Compliments of
Edward F. Malone

THE JOHNS HOPKINS HOSPITAL REPORTS

MONOGRAPHS. NEW SERIES No. VI

THE NUCLEI TUBERIS LATERALES AND THE SO-CALLED GANGLION OPTICUM BASALE

BY

EDWARD F. MALONE

(From the Anatomical Laboratory of the University of Cincinnati)

Illustrated—15 Plates

BALTIMORE
THE JOHNS HOPKINS PRESS
1914

[Copyright, 1914, by The Johns Hopkins Press]

INSTITUTE OF NEUROLOGY

The
ROCKEFELLER
MEDICAL LIBRARY

CONTENTS.

PAGE

I. Introduction 1
II. Material 3
III. Pars Mammillaris Hypothalami 4
IV. Ganglion Opticum Basale 7
A. Location and extent of the ganglion opticum basale
1. Man 8
2. Macacus rhesus 11
3. Lemur rufus 11
4. Cat 12
B. Cell type of the basal optic ganglion 13
C. Separation of the basal optic ganglion from surrounding cell groups through differences in cell character 14
V. Nuclei Tuberis Laterales 18
A. Location and extent of the nuclei tuberis laterales
1. Man 19
2. Macacus rhesus 21
B. Separation of the nuclei tuberis laterales from surrounding cell groups through differences in cell character 21
VI. Relationship of the Various Cell Groups to One Another 23
VII. Conclusion 27
VIII. Literature 31
IX. Bibliography 38
X. Explanation of Illustrations 39

ROSENSTIEL MEDICAL LIBRARY
INSTITUTE OF PHYSIOLOGY
CLASS HIST N
ACCN. 5003
SOURCE recal
DATE

THE NUCLEI TUBERIS LATERALES AND THE SO-CALLED GANGLION OPTICUM BASALE.

By EDWARD F. MALONE.

(From the Anatomical Laboratory of the University of Cincinnati.)

There is perhaps no region of the mammalian brain concerning whose cell groups less is known than that portion of the telencephalon known as the pars optica hypothalami. The cell groups which constitute the subject of this article are so vague and so hopelessly confused in the literature that it is not even possible to determine whether the names basal optic ganglion and nuclei tuberis should be applied to different cell groups or to different portions of the same cell group. In this article it will be shown that these names should be applied to entirely different cell groups; moreover the location and extent of the two cell groups will be described in different mammals, together with a consideration of their relation to surrounding groups of cells, and it will be shown that these two cell groups under consideration are composed of cells of radically different character through which each group may be readily distinguished from the other and from the surrounding cell groups. In addition the cell groups of the pars mammillaris of the hypothalamus will be described.

When we consider the methods employed by most of those who study the anatomy of the mammalian brain perhaps it will not be surprising to realize that the best description of the basal optic ganglion and the nuclei tuberis is that of Kölliker published in 1896, however faulty and confusing this description may be. The reason for this lack of information concerning these cell groups is that most workers are interested in the course of fiber tracts, and their interest in the structure of the nervous system is for the most part limited to the largely mechanical subdivisions revealed by fiber stains; in such preparations the course of fiber systems may often be followed, or at least they reveal certain architectural differences of various regions which serve the purpose of orientation. When preparations in which the cells are stained are studied these preparations are for the most part regarded as showing merely the negative picture of the fiber preparations, and the same

topographical regions are observed, the cells being stained instead of the fibers. When the cell character is noted it is done usually in a superficial manner and principally for the purpose of orientation, and with no purpose of bringing the cell character into relation with a definite function.

The same lack of attention to the cell type is apparent even in the work of the relatively few investigators who employ the experimental methods of Nissl or von Gudden. The following instance is a good illustration of the value of carefully noting the cell character of various cell groups. In his excellent study of the dorsal (sympathetic) nucleus of the vagus nerve Molhant had shown that all the cells of this cell column give origin to all of the vagus fibers which supply smooth muscle and heart muscle, and that certain portions of this cell column supply smooth muscle while a definite portion supplies heart muscle, but he did not attempt to show that a definite type of cell was involved in the innervation of each of these two types of muscle; after studying the vagus sympathetic nucleus I was able to show that the portions of the nucleus which supply smooth muscle and heart muscle may be readily distinguished by the fact that they are composed of cells of different types, and that just as heart muscle is histologically intermediate between smooth muscle and striated muscle, just so the cells of the vagus sympathetic nucleus which supply heart muscle are of a histological character intermediate between that of the cells which supply smooth muscle and striated muscle. Such an observation of the relation of cell type to cell function enables us to locate accurately a functional center even though its cells be mixed with those having a different function, and homologous centers may be recognized in different animal forms; at the same time it emphasizes the necessity of carefully noting the cell character of each cell group, so that even if the function is unknown the presence of a definite cell type will offer a problem for future experimental work, and in the meanwhile preclude the possibility of confusing this cell group with surrounding cells. These differences in cell type are of course most definite in the higher mammals and especially in man, where the various cell groups are highly specialized.

The foregoing consideration of the failure of workers on the anatomy of the mammalian brain to attach sufficient importance to the different types of cells explains why such characteristic cell groups as the basal optic ganglion and the nuclei tuberis have not been clearly separated

from one another and from the surrounding cell groups. The unfortunate condition which here exists is present also in many other regions of the nervous system, and I have considered the tendency of the anatomical work on the mammalian brain somewhat at length not merely as an interesting explanation for our present want of definite information, but because this tendency contains a serious defect whose results are most evident and far reaching, a defect which should be corrected.

The tendency of neurological workers to attach little importance to differences in cell character I have criticised, not only at this point but also later in this article. On the other hand I have no intention whatever of disparaging the ability of other authors, nor am I unappreciative of the excellence, in many cases, of their work and of the valuable results which they have contributed. My criticism is aimed exclusively at the almost universal belief that the various differences in cell type in the nervous system are, after all, of no great importance, and that we should reserve our efforts to discover the connections of various portions of the nervous system. It would be unfair to blame authors for being influenced by a belief so general; moreover it is only comparatively recently that we have begun to employ methods capable of revealing the striking differences in cell character, and only in recent years has the development of cytology given an added stimulus to the careful study of the nerve cell. Above all I wish to disclaim any belief that the method herein employed—that of setting aside groups of cells of an identical type and of comparing such cell groups and of attempting to discover the correlation between cell type and cell function—is of any more value than many other methods of investigation. I advocate it not to displace other methods, but to complement them and add to their usefulness.

Material.

The material studied consists of the following complete series: four of man, one of macacus rhesus, two of lemur rufus, and three of the cat. The tissue was in each case fixed in 95 per cent alcohol, and after dehydration and treatment with chloroform embedded in paraffin. The sections were stained in a one per cent aqueous solution of toluidin blue (Grübler), differentiated in 95 per cent alcohol, dehydrated in absolute alcohol, cleared in xylol, and mounted in Canada balsam.

Pars Mammillaris Hypothalami.

Before proceeding to describe the cell groups of the pars optica hypothalami (telencephalon) it will be necessary to consider those of the pars mammillaris hypothalami (diencephalon), since the cell groups of these two subdivisions of the hypothalamus are most intimately related and cannot be intelligently studied separately. In 1910 appeared my monograph "Über die Kerne des menschlichen Diencephalon" in which the cell groups of the pars mammillaris hypothalami of man were described, together with a brief consideration of certain closely related cell groups of the pars optica. Since the publication of this monograph I have studied both portions of the hypothalamus in the monkey, lemur and cat, and have compared the cell groups observed in these animals with homologous groups found in man. The following description of the cell groups of the pars mammillaris of the monkey, lemur and cat is accordingly original and I should like to call especial attention to the illustrations which clearly show for the first time the different cell groups in macacus rhesus (Figs. 19 to 25). In Series D of man these cell groups are also well shown (Figs. 11 to 18). The other series do not show much of the pars mammillaris, since it did not appear advisable to add many illustrations to show exclusively portions of the pars mammillaris which are not intimately related to the pars optica. In the series of macacus and the Series D of man the plane of section is such as to include this caudal portion of the pars mammillaris. Moreover the dorsal portion of the pars mammillaris has not been illustrated, not only because it has no close relation to the pars optica but also because the thalamus of the three lower forms must first be studied. Certain types of cells also which on account of their location could not be confused with the cells of the pars optica have not been illustrated. Accordingly it appears best to defer such numerous and elaborate illustrations until the whole diencephalon can be included, and to limit the illustrations of the present article to those portions of the pars mammillaris which are closely related to the pars optica.

In studying the anatomy of the cell groups of the diencephalon nowhere are more satisfactory results obtained than in the hypothalamus (pars mammillaris). The great difficulties encountered in attempting to homologize the cell groups of the thalamus of different mammals disappears when we reach the hypothalamus. This is due to the fact that the thalamus is phylogenetically a much more recent

portion of the brain and its development is largely dependent upon that of the rapidly developing pallium. So small is the difference in the cell groups of the hypothalamus of the various mammals studied that for the purposes of this article one description will suffice for all. The pars mammillaris hypothalami is divided into the following primary nuclei (groups of cells having an identical histological character) :

1. Ganglion mediale corporis mammillaris.
2. Nucleus intercalatus corporis mammillaris.
3. Nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
4. Nucleus paraventricularis hypothalami.
5. Corpus hypothalamicum (Luysii).
6. Substantia reticularis hypothalami.
7. Substantia grisea ventriculi tertii.

At this point it is advisable to read the explanation of the various kinds of illustrations as given on pp. 39-40 ; otherwise the figures, some of which are immediately to be referred to, might not be correctly interpreted.

1. Ganglion mediale corporis mammillaris.

This cell group constitutes the greater portion of the mammillary body, and extends further caudally than the other two groups. It is shown in the series of macacus (Figs. 19 and 20) and in the Series D of man (Fig. 11) ; no description of its relations will be given. Concerning its cells it will suffice to state that they are of a type readily distinguishable from the other two groups of the corpus mammillare.

2. Nucleus intercalatus corporis mammillaris.

This is a small circumscribed cell group, described by me in 1910, which lies between the medial and so-called lateral ganglion of the mammillary body. Its location may be seen in the same figures that show the medial ganglion (see above). Later Friedemann found this group in cercopithecus and adopted the name here employed. The cells of the nucleus intercalatus are readily distinguished from those of the two other groups of the mammillary body through their characteristic type; especially in man they have the relatively large and discrete Nissl granules characteristic of efferent nerve cells. This cell group should not be confused with groups which are occasionally mechanically split off from the medial ganglion by fiber masses; the difference in cell type renders this distinction easy.

3. Nucleus tubero-mammillaris.

The cells of the so-called lateral ganglion of the corpus mammillare may be readily followed orally and laterally into the angle between the pes pedunculi and the tractus opticus, whereas orally and dorsally they may be followed through many sections accompanying the tractus thalamo-mammillaris and the columna fornicis. To this complex of cells having an identical histological character I gave (1910) the name "nucleus mammillo-infundibularis," a name which Friedemann (1911) has adopted in his article on the diencephalon of cercopithecus. It is evident that this name is unsuitable, since the cell group is not situated in the infundibulum, and I have therefore changed it to "nucleus tubero-mammillaris." The nucleus tubero-mammillaris is shown in all the series illustrated and its relation to the basal optic ganglion and the nuclei tuberis may be readily seen. (Since the figures were drawn and labeled before I decided to change the name of this nucleus, it appears on the outline drawings as "nucleus mammillo-infundibularis," but wherever space has permitted the new name has been added in parentheses. The explanation of each plate is so arranged as to remove any possibility of confusion.) The character of its cells in the different forms is illustrated in Figs. 41, 47, 52 and 57. The relation of this nucleus to the basal optic ganglion will be discussed later. It should be noted that a portion of this nucleus is situated in the pars optica.

4. Nucleus paraventricularis hypothalami.

This characteristic column of cells is situated partly in the pars mammillaris but principally in the pars optica. Its location is shown in all the series, and the character of its cells in Figs. 43, 49, 54 and 58. In man this nucleus was first described by me in 1910, and the fact that such a striking cell group had not been previously described in man is probably due to the almost exclusive use of fiber stains. In 1911 Friedemann found this cell group in cercopithecus. It is certainly homologous with the group described by Cajal in rodents under the name of "núcleo subventricular," and with that described by Ziehen in marsupials as "Nucleus subcommissuralis." Homologous groups are also possibly found in vertebrates even as low as the fishes. The nucleus paraventricularis is intimately related to the basal optic ganglion and also to the nucleus tubero-mammillaris as these three nuclei

appear to be components of one large cell complex, and while differing from one another, differ much more from the surrounding cells. These relations will be discussed later in detail.

5. Corpus hypothalamicum (Luysii)

This is such a compact, isolated cell mass, and is situated at such a distance from the basal optic ganglion and the nuclei tuberis that no description is necessary; it has been included in the illustrations, however, for the purpose of orientation.

6. Substantia reticularis hypothalami.

This group of cells on account of its position need not be considered in this article. A description will be found in my monograph on the diencephalon. Many of its cells are of a motor type of structure, and these together with the cells of the nucleus intercalatus of the corpus mammillare are the only cells of the entire diencephalon which show the histological character peculiar to motor cells.

7. Substantia grisea ventriculi tertii.

This cell mass is shown in all series and the cell type in Figs. 40, 46, 51 and 56. The greater portion lies in the pars optica, and it should be noted that dorsally and laterally the cells are less densely packed than ventrally and medially. The substantia grisea is closely related to the nuclei tuberis, and this relation will be fully discussed in connection with the description of the nuclei tuberis.

If we now observe in the illustrations the location and extent of the different cell groups previously described and note also the character of their cells in the different mammals, we shall be prepared to understand the following description of the basal optic ganglion and the nuclei tuberis and the consideration of the relations of the latter two nuclei to the former.

Ganglion Opticum Basale.

The name ganglion opticum basale was given with the intention of implying a function which this cell group almost certainly does not possess; on the other hand this name effectively distinguishes this cell group from the nuclei tuberis with which it has been confused. Since the so-called basal optic ganglion is such a characteristic cell group, and

since the homologous groups in various mammals are so constant both as to location, extent and cell character, it appears highly probable that we shall not have to wait long before this name may be abandoned for one which will indicate its true function, and until then it seems better not to introduce a temporary name implying merely some morphological character. In arriving at the function of a cell group the first essential (and probably the most important of all) is to clearly distinguish it from the surrounding cell groups and to study carefully its relations to such cell groups; in this article I shall endeavor by means of illustrations and description to make the resulting picture of the so-called basal optic ganglion so definite that its confusion with all other cell groups will be impossible, and if this result be obtained there need be little concern as to the fitness of the name employed.

Location and extent of the ganglion opticum basale.

MAN.

The basal optic ganglion in man is a mass of gray matter, superficially situated partly in the tuber cinereum and partly in the anterior perforated substance, which extends along both borders of the optic tract. The main mass of cells forms in the anterior perforated substance a column which is closely applied to the dorsal portion of the oro-lateral surface of the optic tract. This mass is connected by a comparatively small number of scattered cells situated directly dorsal to the tract with another cell mass which follows in the tuber cinereum the caudo-medial border of the optic tract; in other words the basal optic ganglion consists, generally speaking, of two parallel columns of cells lying along either side of the optic tract, which are connected by scattered cells of the same type lying dorsal to the optic tract. For the second time I strongly recommend a consideration of pp. 39-40, where it is pointed out just what each type of illustration is intended to show.

Taking up the first series of man (Series AC) the basal optic ganglion appears caudally in Fig. 4 as a few scattered cells situated on the periphery of the tuber cinereum; Figs. 5 and 6 show the development of the cell mass as we pass orally. The cell masses shown in Figs. 4 and 5 are to be regarded as a caudal projection of the cell column lying along the caudo-medial border of the optic tract, and are continuous with the caudal portion of this cell column which appears first in Fig. 6. Between Figs. 6 and 7 is a considerable gap, in which the following

changes have occurred: as the optic tract approaches the median plane and applies itself to the base of the brain the cell mass continues to increase in size, extending further laterally and also to a less extent further medially, and assumes a position as a column on the dorsal surface of the caudo-medial aspect of the optic tract, or in other words it extends in the tuber cinereum along the line where the tuber joins the optic tract. Midway between Figs. 6 and 7 the medial pole of the column crosses the median line and caudal to the optic chiasm unites with the corresponding column of the other side by means, however, of only a few scattered cells situated in the infundibulum. The next series (D) shows this fact. But still another change has occurred between Figs. 6 and 7, namely, after reaching its greatest development, which, as previously described, occurs at the juncture of the tuber cinereum with the caudo-medial border of the optic tract, the cell mass becomes rapidly diminished to only a few scattered cells which are situated on the dorsal (or deep) surface of the optic tract. Fig. 7 shows the extent of the basal optic ganglion slightly oral to this region of its poorest development; the section passes through the optic tract near its oro-lateral border and since the section is near this border the cell mass has increased in extent. Between Figs. 7 and 8 it increases steadily in size to reach its maximum in Fig. 8; this figure represents a section through the cell column which extends in the anterior perforated substance along the oro-lateral border of the optic tract. In Fig. 9 the basal optic ganglion has diminished in size, and this is due to a shortening of the lateral portion of the column; that the lateral portion of the column should be shortened is evident when we recall that the cell column lies parallel to the optic tract, and that the course of the optic tract is such that in the present plane of section as one proceeds orally the lateral portion of the tract appears and disappears first (see Figs. 1 to 10). Fig. 10 shows the most oral portion of the basal optic ganglion. The fact that the portion of the ganglion situated caudal (medial) to the optic tract does not extend as far laterally as that portion situated oral (lateral) to the tract should be correlated with the difference of the relation of the two borders of the tract to the base of the brain; for while the oral (lateral) border of the tract is in intimate relation to the anterior perforated substance from the chiasm to a point far lateral from the median plane, the caudal (medial) border of the tract is in intimate relation to the tuber cinereum, which extends for

a shorter distance laterally, and then the tract passes over the crus cerebri, where of course it is no longer in relation to gray matter.

To sum up, Series AC of man (Figs. 4 to 10) shows, in sections almost parallel to the course of the optic tract, the appearance of the three parallel columns of cells which constitute the basal optic ganglion; one column lies in the tuber cinereum along the medio-caudal border of the optic tract, the second extends along the dorsal (deep) surface of the tract and consists of only a few cells, while the third and largest column extends in the anterior perforated substance along the latero-oral border of the tract. The caudal column is continuous in the infundibulum with the corresponding column of the opposite side. The figures show the inevitable relation of three parallel columns in slightly oblique section.

Series D of man (Figs. 11 to 18) shows essentially the same relations, but the plane of section is different. In the previous series the plane was almost parallel to the course of the optic tract, although slightly approaching the plane of a cross section; in Series D the plane of section is almost at right angles to the course of the optic tract, and both the caudo-medial and the oro-lateral borders are shown in all sections. It is evident that a plane of section at right angles to the median plane (which would cut both halves of the brain symmetrically) could not pass through the optic tract at right angles to its course, since the two tracts converge towards the median plane as they pass orally; therefore to obtain a cross section of the right tract the plane of section must lie more oral on this side than on the left. The asymmetry of the plane of section of Series D is not quite great enough to produce a cross section of the right optic tract, although this condition is very nearly attained.

When Fig. 11 of Series D is compared with Fig. 4 of Series AC the location of the basal optic ganglion is rather confusing, for in the latter series it appeared caudally in the tuber cinereum near the medio-caudal border of the optic tract, while in Fig. 11 it appears first in the anterior perforated substance along the oro-lateral border; if we keep in mind the asymmetry of the section, and the fact that the cell column here shown extends further laterally than the other two columns of the cell group and that in such asymmetrical sections the lateral portion is the most oral, little difficulty should exist in realizing just why this one of the three cell columns should appear first. Fig. 12 shows practically the same relations, except that the optic tract is nearer the median

line. In Fig. 13 the cell column along the medio-caudal border of the tract, as well as the scattered cells dorsal to the tract, appears, and from here throughout the entire series these three columns are present. Of course all columns are in cross section. In Fig. 18 the cell mass is seen to extend across the median line, a condition which occurs also in the three other series of man. Series D (Figs. 11 to 18) shows clearly that the basal optic ganglion consists of two well developed parallel columns of cells connected by an intermediate parallel column consisting of only a few cells. As will be shown later the exact extent of the basal optic ganglion in all the mammals studied is readily determined by the distinctive histological character of its cells, and accordingly the three parallel cell columns have been considered as merely subdivisions of one nucleus, not because this seems convenient, but because the identical character of their cells makes such a conclusion unavoidable.

MACACUS RHESUS.

In macacus rhesus the basal optic ganglion is shown first in Fig. 22, although it extends slightly further caudally. In this figure the ganglion is situated just oral to the line of apposition between the tuber cinereum and the optic tract. In the sections between Figs. 22 and 23, as we pass orally, the cells become reduced in number and lie dorsal to the tract, and as the oro-lateral border of the tract is reached increase in number. In Fig. 23 appears the cell column which lies in the anterior perforated substance along the oro-lateral border of the tract. The further development of the ganglion (Figs. 24 and 25) needs no description. In Fig. 22 the medial pole of the ganglion is seen to approach the median line, and between Figs. 22 and 23, just caudal to the optic chiasm, a very few widely scattered cells unite the ganglia of opposite sides. As in man the basal optic ganglion in macacus is seen to consist of the same three parallel columns of cells, of which the oro-lateral column (situated in the anterior perforated substance) constitutes the greater part of the ganglion.

LEMUR RUFUS.

The basal optic ganglion of the lemur does not differ essentially from that of man and macacus, except that whereas in the two latter animals it consisted of two parallel cell columns loosely connected by a third, in the lemur this connecting mass of scattered cells (dorsal to

the optic tract) is missing; consequently the ganglion consists of two entirely separate parallel columns of cells. Fig. 27 represents a section between the two cell columns. As in man and macacus the ganglia of opposite sides are united by a very few cells; this union occurs just caudal to the optic chiasm (slightly caudal to the level represented in Fig. 27).

CAT.

The basal optic ganglion in the cat (Figs. 31 to 35) has practically the same location and extent as in the lemur. As in the lemur the ganglion consists of the same two parallel cell columns, which are completely separate. Between Figs. 32 and 33 lies the region in which the ganglion is absent. Just caudal to the optic chiasm (caudal to level of Fig. 33) the ganglia of opposite sides are united in this series by a few cells; in the other two series of the cat no union was present.

Comparing the location and extent of the basal optic ganglion in all four animals the following facts should be noted:

1. The basal optic ganglion in all four animals consists almost exclusively (in some cases exclusively) of two compact, parallel cell columns. The larger of these two columns lies superficially in the anterior perforated substance along the line where this region becomes continuous with the oro-lateral border of the optic tract; the smaller column lies superficially in the tuber cinereum along the line where it joins the optic tract.

2. These two constant, parallel cell columns are united in man, and to a less extent also in macacus, by more or less diffusely scattered cells of the same type which lie dorsal to the optic tract.

3. In all four forms there occurs a union of the ganglia of opposite sides by means of diffusely scattered cells located just caudal to the optic chiasm. In man this union is very definite, in macacus less definite, while in the other two animals it is rudimentary and due to the presence of a very few widely scattered cells between the two ganglia. In the cat even this feebly developed fusion is not present in all individuals.

4. Although the phylogenetic series from man to the cat is too short to be of much service in revealing the phylogenetic development of so constant a cell group as the basal optic ganglion, it is apparent that as we descend the series the two parallel cell columns become separate (more closely united in man than in macacus, and separate in the lemur

and cat); the same is true as to the fusion of the ganglia of opposite sides (definite in man, less so in macacus, barely present in the lemur and not always present in the cat.)

Cell type of the basal optic ganglion.

It is not my intention to attempt to give in words the characteristics of the cells of the basal optic ganglion which have been already satisfactorily shown in the illustrations. I shall confine myself to pointing out the fundamental characters of these cells, and when we have thus become familiar with the main features of the cell picture we shall be in a position to discuss the relations of these cells to those of other groups. The water color reproductions of the cells of the basal optic ganglion, and of all other cells thus illustrated (Figs. 38 to 58), were all drawn from cross-sections of the brain. In Series D of man, in which the plane of section differs widely from that of a cross-section, I have been unable to observe any important difference in the appearance of the cells of the basal optic ganglion, and it is my opinion that the plane of section does not affect to any appreciable extent the appearance of the majority of these cells. The cells of the basal optic ganglion and of all other groups illustrated are as characteristic in Series D as in Series AC. However, I have not made a careful enough study of this point to state definitely that the cell character is absolutely unaffected by differences in the plane of section. The cells of the basal optic ganglion in all four animal forms (Figs. 38, 44, 50 and 55) are large polygonal cells which possess very coarse processes. These processes, as is shown in Fig. 37, form an intercellular feltwork; under low power one would hardly suppose that this feltwork was composed of cell processes, and the ganglion appears to be characterized not only by its typical cells but also by the presence of a distinctive intercellular substance. These processes are practically colorless, and are in Fig. 37 represented as blue because at this magnification they could not be shown in any other manner. The cell processes in Figs. 38, 44, 50 and 55 are not as long as they appear in the actual preparations. Another fundamental character of these cells is the distribution of the Nissl substance, nearly all of which is massed on the periphery of the cell; this peripheral distribution is not equal in all portions of the periphery, since the depth is much greater at certain points, and at other points of the periphery the Nissl substance may be almost entirely absent.

Of course the distribution of the Nissl substance will appear different according to the location of the optical section, and the figures show this to some extent, although they represent to a certain extent a combination of different optical sections. Although minor differences in cell character exist in different animals, the cell group is phylogenetically so old that in the relatively brief interval between man and the cat no changes in cell character have occurred which are sufficiently fundamental to permit of correlation with the phylogenetic position of the corresponding animals; this point will be discussed later in connection with the nuclei tuberis, where such a relation between cell character and the phylogenetic position of the corresponding animal actually exists. The structure of the cells of the ganglion opticum basale is such as to exclude the possibility of these cells being motor, whereas the large size of the cells probably indicates (as Dr. Donaldson has suggested to me) that they either receive impulses converging from many sources or distribute impulses over an extensive region.

Separation of the basal optic ganglion from surrounding cell groups through differences in cell character.

A subdivision of any portion of the nervous system based merely upon the splitting up of gray matter through the mechanical agency of fiber masses is, except in certain cases, valuable merely with reference to orientation; such a subdivision should therefore be considered as a crude (although necessary) beginning to be followed by a more careful study of the region involved in which the cell character of the various groups receives careful attention. Moreover it is highly unsatisfactory for an author to state dogmatically that he recognizes the presence of certain cell groups upon the basis of certain differences of cell character, concerning which he is either silent or else treats in a superficial manner; for we are left in doubt as to whether these differences in cell character are really fundamental, and as to the degrees of relationship between the cell characters of various cell groups. When we have described the location and extent of various cell groups and have made it possible to recognize this by means of a definite cell type, and when we have clearly shown the differences and similarities in cell character of various cell groups, and have pointed out the phylogenetic development and relations of these groups, then and not until then will there be a basis for experimental work which will help solve many important

questions as to the elementary mechanisms of the nervous system. In the case of the basal optic ganglion, therefore, I shall not be content with having pointed out its location and extent, but shall proceed to compare the character of its cells with that of the cells of surrounding groups; such a comparison serves not only to set aside this cell group as different from other cell groups by virtue of differences in cell character, but it enables us also to recognize certain similarities of cell character between the cells of the ganglion and the cells of other groups, so that different degrees of relationship between the different cell groups may be provisionally stated.

I shall first point out the differences in cell character between the cells of the basal optic ganglion and those of the surrounding groups so as to complete the picture of this cell group; afterwards the relations of various cell groups will be discussed (but not until the nuclei tuberis have been described). There is no difficulty in distinguishing the cells of the basal optic ganglion from those of the nuclei tuberis and of the substantia grisea ventriculi tertii. This is shown by a reference to the corresponding figures 38, 39 and 40; 44, 45 and 46; 50 and 51; 55 and 56; moreover the difference between the cells of the basal optic ganglion and those of the substantia grisea is well shown in Fig. 37.

The cells of the basal optic ganglion may be readily distinguished also from those of the nucleus tubero-mammillaris, although both types of cells have a certain similarity; the failure to recognize the unity of the cell complex known as the nucleus tubero-mammillaris (mammillo-infundibularis) and to clearly separate it from the basal optic ganglion is one of the most important causes for our meager knowledge of this region. Considering first the relations of these two cell groups as to location, it is evident from the illustrations that they are closely related only for a short distance. Moreover the cells of the nucleus tubero-mammillaris are for the most part rather diffusely scattered, while those of the basal optic ganglion are densely packed together and the cell group is further characterized by the intercellular feltwork formed by the coarse colorless cell processes; these two points may be observed by comparing Figs. 36 and 37. Comparing the cell type of the two cell groups the fundamental difference found in all four animals involves the appearance of the Nissl substance; in both forms the Nissl substance is located principally on the periphery of the cell, but in the cells of the basal optic ganglion the massing of the Nissl substance on the periphery

is extreme, whereas in the cells of the nucleus tubero-mammillaris the Nissl substance is not so densely packed together on the periphery and more of it is present in the central portion of the cell. In other words the Nissl substance in the cells of the nucleus tubero-mammillaris is more diffusely distributed throughout the entire cell. The difference in cell type obtains throughout the entire extent of both nuclei. A study of the illustrations shows that while other differences in cell type occur in certain animals the fundamental difference consists in the mode of distribution of the Nissl substance (Figs. 38 and 41; 44 and 47; 50 and 52; 55 and 57).

The separation of the basal optic ganglion from the nucleus paraventricularis hypothalami on the basis of cell type is difficult. Fortunately both are in all four animals sharply circumscribed, and although the extremities of these two cell columns approach one another (Fig. 10), they never actually fuse. A study of the location of these two cell groups will show their axes are almost at right angles to each other. In a former article I made the statement that the cells of the basal optic ganglion in man could not be distinguished from those of the nucleus paraventricularis, but a more careful study of the cell groups in man together with their study in other animals proves that this statement is not correct, although not far from the truth. As a matter of fact I have been unable to observe any one fundamental difference between these two types of cells which is clearly shown in all four animal forms, although in each animal some differences are present which always make a distinction possible. There is one difference which holds fairly well for all forms, and this is the same difference that was so evident between the cells of the basal optic ganglion and those of the nucleus tubero-mammillaris, namely, the Nissl substance is more densely massed on the periphery of the cell in the case of the basal optic ganglion, while in the cells of the nucleus paraventricularis the Nissl substance is more uniformly distributed throughout the cell. In man (Figs. 38 and 43) this difference is not marked, but in the basal optic ganglion (Fig. 38) the Nissl substance on the periphery forms in part large, irregularly placed masses of granules, while in the cells of the nucleus paraventricularis (Fig. 43) the granules are smaller, more uniform in size and do not stain so intensely; at the same time the central portion of the cell is somewhat more deeply stained (due to more Nissl substance) than in the case of the cells of the basal optic ganglion. Other differences in man are as follows: the cells of the basal optic

ganglion are somewhat larger (the smallest cell illustrated in Fig. 38 shows only a small portion of a cell in optical section), the nuclear membrane is not so definite, and the nucleus is larger. In macacus (Figs. 44 and 49) the difference in distribution of the Nissl substance is less than in any of the other animals, but even here the Nissl substance in the cells of the basal optic ganglion is more nearly confined to the periphery, is denser here and not so dense in the interior portion of the cell as in the case of the other cell group; this results in a sharper differentiation between peripheral and central portions of the cell in the case of the basal optic ganglion. Other differences in macacus are: the cells and cell nuclei of the basal optic ganglion are smaller than those of the nucleus paraventricularis (the opposite is true in man), and the cells of this latter nucleus are rather piriform. In the lemur (Figs. 50 and 54) the difference in distribution of the Nissl substance is marked, the differentiation of the cell into peripheral and central portions being much sharper in the cells of the basal optic ganglion. In the cat (Figs. 55 and 58) the difference between periphery and center of the cell is again more marked in the cells of the basal optic ganglion, since in the cells of the other group the central portion of the cell (including the cell nucleus) stains deeply (Fig. 58). Note also in the cat that, just as in man, the cells of the basal optic ganglion are larger, but unlike those of man have smaller cell nuclei than the cells of the nucleus paraventricularis.

The resemblance of the cell type in the case of the basal optic ganglion and the nucleus paraventricularis hypothalami is therefore very close, but in all four animals studied the cells of the basal optic ganglion were found to be more sharply differentiated into a peripheral zone containing dense masses of Nissl substance and an inner portion relatively free from this substance, whereas in the cells of the nucleus paraventricularis hypothalami the Nissl substance was not so sharply differentiated as to its distribution. It will be recalled that within the cells of the nucleus tubero-mammillaris this differentiation was even less marked than within those of the nucleus paraventricularis.

Another cell group must be distinguished from the basal optic ganglion. This is the nucleus ansae peduncularis of Meynert (ganglion basale of Kölliker). It occurs in man, macacus and the lemur, but I was unable to find it in any of my three series of the cat. Its location and extent may be seen in the different illustrations. In all three animals in which it occurs it is readily distinguished from the basal

optic ganglion by the large size of its cells. In man, as was pointed out by Kölliker, the cells of the ganglion basale may be readily separated from those of the basal optic ganglion by the fact that they are heavily pigmented (Fig. 42). In a previous article I have discussed the value of pigmentation as a basis of distinguishing different cell types. Yellow pigment occurs in certain nerve cells of the adult human and increases with age, but this occurrence and increase in amount is not erratic, but behaves differently with respect to different types of cells. Some types of cells never contain pigment, others always contain it, while still other types may contain none or under other conditions may contain a small or even a moderate amount. But however the total amount of yellow pigment in the brain of different adults may vary, the amount in each specific type of cell retains the same relation to that of every other type of cell; in other words, the relative amount of pigment in the different types of cells is constant in all individuals. Note that this pigmentation of the cells of the ganglion basale in man is accompanied by an additional characteristic (large size) and that the homologous cells of macacus and the lemur are entirely different from those of other cell groups, although pigmentation is of course lacking. This question of the relative amount of yellow pigment as a characteristic of certain types of cells which differ also in other respects will be noted again in connection with the nuclei tuberis. This yellow pigment should not be confounded with the brown pigment which occurs in the cells of the substantia nigra and elsewhere.

Now that the differences in cell type between the cells of the basal optic ganglion and those of surrounding groups have been studied it would be desirable to consider the relationship of these various cell groups from the standpoint of similarities in cell character. This consideration, as well as that of the literature, must however be postponed until the nuclei tuberis have been described, since such a comparison of the various cell groups demands a familiarity with the nuclei tuberis and the substantia grisea of the third ventricle.

Nuclei Tuberis Laterales.

Under the name of nuclei tuberis laterales I shall describe certain cell groups of the pars optica hypothalami (telencephalon) which I have formerly considered very briefly in my monograph on the human diencephalon. Although a number of authors have written of nuclei

tuberis, except in one case, there is absolutely no reason to believe that any of them have had in mind the characteristic nests of cells which will now be described. Kölliker undoubtedly saw these nuclei, although, as will appear later, his description is faulty and his figures incorrectly labeled; the result is so confusing that a careful study of this region is necessary to appreciate the value of Kölliker's observations. In the previous brief description I employed the name nuclei tuberis, but in the present article adopt the name nuclei tuberis laterales. The name nuclei tuberis is not distinctive and might be used to indicate any cell group whatsoever located in the tuber cinereum; as a matter of fact it has been so used, and the resulting confusion may be imagined when one considers how many different cell groups lie in the tuber cinereum. This confusion is not one merely of names, but involves the failure to distinguish (regardless of names) various cell groups of the tuber cinereum which in properly prepared material may be readily distinguished not only through differences in location but also through striking differences in cell type.

Location and extent of the nuclei tuberis laterales.

The nuclei tuberis laterales consist in man and macacus of several nests of cells located on the periphery of the tuber cinereum. In the lemur in this location one sees the beginning differentiation of these cell groups from the cells which surround them, although these differences are so slight that I have not attempted to show them in the illustrations. In the cat these cell groups are absent.

MAN.

In Series AC of man the nuclei tuberis laterales are shown in Figs. 1 to 8; the size of the cells, however, has been so much reduced that they should be examined with the aid of a hand lens. In Fig. 1 two indentations are shown on the base of the brain which should be noted. One indentation marks off on the base of the brain the medial boundary of the pes pedunculi, while the more medial indentation forms the superficial boundary between the tuber cinereum and the nucleus tubero-mammillaris (nucleus mammillo-infundibularis), this nucleus lying between these two fissures. The area bounded by these two fissures ventrally, and by the columna fornicis dorsally, is of especial importance in describing the location of the nuclei tuberis.

On examining Figs. 1 to 6 these two fissures are seen to be practically parallel, and the area bounded by them and by the fornix column undergoes as we pass orally the following change: in the caudal portion (Fig. 1) this area is occupied by the cells of the nucleus tubero-mammillaris, whose caudal pole constitutes the lateral ganglion of the mammillary body; passing further orally these large cells are replaced (especially those situated ventrally and medially) by the small cells of the nuclei tuberis laterales and of the substantia grisea. Accordingly the caudal portion of this region is continuous with the lateral ganglion of the mammillary body, whereas orally it gradually becomes the lateral portion of the tuber cinereum. In this region included between these two fissures ventrally, the pes pedunculi laterally, and the fornix column dorsally, lies by far the greater portion of the cells of the nuclei tuberis laterales. Referring to Figs. 1 to 8 the location and extent of these cell groups are evident, and only a few comments will be necessary. The nuclei tuberis laterales consist of a variable number of well circumscribed nests of small cells, and can be distinguished even without the aid of their characteristic cell type. These different cell nests are more or less connected with one another, and their separation is to be regarded probably as dependent upon the mechanical influence of fiber masses, since their partial fusion, identical cell type, and variable number would seem to exclude the possibility of these separate groups having different functions. The cell nests of the nuclei tuberis laterales are practically free from cells of surrounding groups.

In considering the second series of man (Series D, Figs. 11 to 15) it is absolutely essential to understand the plane of section; this has already been described in considering the basal optic ganglion. It will suffice to point out that Series D differs from Series AC in that the plane of section of the former passes more caudally as it passes from dorsal to ventral; and that in it the opposite sides of the brain are cut asymmetrically, in that the lateral portion of each section of Series D is situated further oral than the medial portion of the corresponding section. As was previously noted the plane of section of Series D is the only one which can pass through the right optic tract at right angles to its long axis; this relation to the optic tract will render a clear picture of the plane of section relatively easy. Bearing this plane of section in mind a study (with the aid of a hand lens) of Figs. 11 to 15 will show that the location of the nuclei tuberis laterales in Series D is practically the same as in the preceding Series AC, Figs. 1 to 8. Of

the two fissures referred to previously, the lateral (just medial to the pes pedunculi) does not occur, since the obliquity of the plane of section is such that it appears only in sections situated further caudally. The medial one of these two fissures, however, appears in every section from Figs. 11 to 15, and as in the other series, forms superficially the medial boundary of by far the greater portion of the nuclei tuberis laterales.

MACACUS RHESUS.

In macacus the location of the nuclei tuberis laterales is similar to that in man, except that in most sections only one cell group is shown, and the cell mass does not invade the medio-ventral portion of the tuber. A comparison of Figs. 19 to 22 (macacus) with Figs. 1 to 8 (man) will show that in both animals the nuclei differ but little as to location. The two parallel furrows on the base of the brain are shown in Figs. 19 and 20.

In both man and macacus the nuclei tuberis laterales have, accordingly, practically the same location, and by far the greater portion is situated in the previously described region; this region, bounded ventrally by the two parallel furrows, laterally by the pes pedunculi, and dorsally by the fornix column, is occupied caudally by the nucleus tubero-mammillaris, and the nuclei tuberis laterales displace this nucleus as one passes orally, and after the optic tract has fused with the tuber, the nuclei tuberis are continued orally in the angle between the pes pedunculi and the optic tract. Since the purpose of this paper is in part to give a foundation for experimental study, it should be noted that *the main cell mass of the nuclei tuberis laterales may be accurately located in the intact brain just beneath the surface of the most lateral portion of the tuber cinereum, between the two parallel furrows and just caudal (medial) to the optic tract.* In toluidin blue sections the nuclei may be distinguished as circumscribed, lightly staining areas by means of the unaided eye. As previously stated no trace of the nuclei tuberis laterales is present in the cat, while in the lemur they are indicated so faintly that it seems best not to attempt to represent them in the illustrations.

Separation of the nuclei tuberis laterales from surrounding cell groups through differences in cell character.

The nuclei tuberis laterales are readily distinguished from the surrounding cell groups not only in that they are sharply circumscribed cell masses having a constant location, but also through their charac-

teristic cell type. A reference to Fig. 36 will serve as an introduction to the further consideration of the differences in cell character. On comparing the cell character of the nuclei tuberis laterales of man and macacus (Figs. 39 and 45) with that of the other cell groups shown in the illustrations it will at once be evident that this cell type differs radically from all others except that of the substantia grisea of the third ventricle (Figs. 40 and 46); this similarity is of importance, and its significance will be considered when the relationship of the various cell types is discussed. Comparing the cell type of the nuclei tuberis laterales in man (Fig. 39) and in macacus (Fig. 45) it is evident that aside from the presence of pigmentation in man (of course not to be expected in macacus) there is no essential difference. The fundamental characteristic of this cell type in both forms lies in the appearance of the cytoplasm, which contains an extremely small amount of Nissl substance in the form of fine granules; the relation of cell nucleus to cytoplasm in respect to volume is also practically the same, although in macacus the cytoplasm is relatively less, a change that is to be expected, as will appear later. In describing the cells of the nucleus ansae peduncularis (p. 18) I pointed out the fact that if two cell groups differ as to the amount of yellow pigment in their cells they will also differ in other respects, and that homologous groups in lower animals (where all pigmentation is absent) will also appear different. Accordingly the presence of densely packed yellow granules in the cells of the nuclei tuberis laterales of man is not the only distinctive characteristic of these cells, but is connected with other characteristics, common also to the homologous cells of macacus; these characteristics involve the appearance of the cytoplasm and make it possible to separate these cells without difficulty from those of surrounding groups. If we study the cell type of the substantia grisea in all four forms (Figs. 40, 46, 51, and 56) we find the cell type practically unchanged, since in all forms the cells of this group are characterized by the extremely small amount of cytoplasm and relatively large nucleus; in many cells the cytoplasm is almost absent, and one sees only a large nucleus and perhaps one or more cell processes.

Accordingly the cells of the substantia grisea may be readily separated from those of all portions of the nuclei tuberis laterales not only through their smaller size, but also through the minute amount of cytoplasm in relation to the size of the cell nucleus; however, on the border line between these two types of cells occur occasionally transi-

tion types, whose significance will be discussed later. The nuclei tuberis laterales must be sharply distinguished from certain regions of the substantia grisea in which the cells are more densely packed together than in other portions of the substantia grisea. Differences in the density of different portions of the substantia grisea may be seen in many sections, and very definite areas of closely packed cells are shown in Figs. 17, 22 and 24. While in such dense masses the cells are possibly somewhat larger than the remaining cells of the substantia grisea, I do not consider the difference in cell type clear enough to justify one in setting aside such dense cell masses as distinct nuclei. Whatever the significance of these denser cell masses of the substantia grisea, one fact is certain: they differ both in location and in cell type from the nuclei tuberis laterales; the radical difference between these two kinds of cell groups should be clearly recognized. Of course the structure of the cells of the nuclei tuberis laterales as well as that of the cells of the substantia grisea is radically different from that of motor cells, while the small size of both types of cells would indicate that the connections of each cell were very limited; this correlation between cell size and the extent of the connections of each cell has already been referred to.

Relationship Of The Various Cell Groups To One Another.

From the previous description of the various cell groups together with a reference to the figures showing their cell types, it will be evident that the cell groups herein considered fall naturally into two classes:

1. Those composed of small cells, including the substantia grisea, and the nuclei tuberis laterales, and

2. Those composed of large cells, including the basal optic ganglion, the nucleus paraventricularis hypothalami, the nucleus tuberomammillaris, and perhaps also the nucleus ansae peduncularis (ganglion basale).

Taking up the first class of nuclei a most interesting relation will be found to exist between the substantia grisea and the nuclei tuberis laterales. The cells of the substantia grisea are the most primitive of the hypothalamus. The constancy of cell type in all four animal forms would suggest this, but the strongest evidence is derived from the nature of the cell type. The cell type of the substantia grisea, with its scanty cytoplasm, resembles that of embryonic cells; it occurs often in

invertebrates; it is the only type in the hypothalamus which approaches that of the neuroglia cells, and transition forms occur concerning which one is in doubt as to whether they are neuroglia cells or cells of the substantia grisea; the cells are most abundant near the ventricle from whose border all cells of the hypothalamus have arisen, while laterally they are replaced by more highly differentiated types of cells. It is by no means certain that all or even any of the cells of the substantia grisea are functional. That the cells of the nuclei tuberis laterales have arisen from those of the substantia grisea is certain; if we look in the lemur at the regions where in higher forms the nuclei tuberis laterales occur, we see that the type of cell is somewhat different from the surrounding cells of the substantia grisea; this difference increases in macacus, and still more in man, while in the cat there is no indication of any new group. It is thus evident that the most recent cell groups of the hypothalamus (nuclei tuberis laterales) have arisen directly from the oldest cell group (substantia grisea), and that new cell groups are not necessarily formed by the further histological differentiation of portions of cell groups which are already highly developed, thus resulting in a very highly differentiated cell type, but that on the contrary new cell groups may arise from cell masses which have remained primitive. In other words the fact that a cell group is of recent origin does not give any information as to the extent of its histological differentiation, since this differentiation depends also upon the development of the cell group from which the new group arises.

In considering the second class of cell groups in the hypothalamus, all of which are composed of large cells, the nucleus ansae peduncularis requires only a brief consideration. The cell type of this cell group differs considerably from that of other groups, and the nucleus is probably of much more recent phylogenetic origin, since I have not as yet been able to find it in the cat; in order to consider the relations of this cell group a study of the neighboring regions of the telencephalon will be necessary, and I shall content myself with having shown that it is clearly distinguishable from the basal optic ganglion, and with having given the relative location of both groups of cells.

Concerning the other three cell groups in this class (basal optic ganglion, nucleus paraventricularis hypothalami, and nucleus tubero-mammillaris), the phylogenetic series from the cat to man is far too short to give such satisfactory results as in the case of the nuclei tuberis laterales, since the former three groups are of much older origin; certain

relationships may, however, be established. Of these three cell groups the basal optic ganglion is composed of cells whose type is by far the most constant in the different animal forms, and the volume of this cell group is reduced in the lower forms to a less extent than is true of the two other nuclei; moreover, while the cell type of the basal optic ganglion approaches closely that of the nucleus paraventricularis, there are no transition forms between its cell type and that of the nucleus tubero-mammillaris or that of the substantia grisea; finally the basal optic ganglion is almost entirely free from the invasion of neighboring cells. All of these considerations make it seem probable that of the three nuclei the basal optic ganglion is the oldest and most highly developed. Closely related to the basal optic ganglion is the nucleus paraventricularis; it is more reduced in size in the lower forms than is the basal optic ganglion; between its cell type and that of the nucleus tubero-mammillaris transition forms occur, and between its cells lie many cells of the substantia grisea. While these facts make it probable that the nucleus paraventricularis is possibly not so old a cell group as the basal optic ganglion, they enable one to state positively that the nucleus paraventricularis is related on the one hand to the basal optic ganglion and on the other to the nucleus tubero-mammillaris. The third cell group, the nucleus tubero-mammillaris, is like the nucleus paraventricularis much reduced in size in the lower animals; it differs strikingly from both the other cell groups in being not sharply circumscribed, but on the contrary is very diffuse, extending through a large portion of the hypothalamus; it is invaded accordingly by the cells of the substantia grisea to a much greater extent than is the nucleus paraventricularis. Finally the cell type of the nucleus tubero-mammillaris shows a transition on the one hand to that of the nucleus paraventricularis and on the other to that of the substantia grisea. Therefore the nucleus tubero-mammillaris, while related to the nucleus paraventricularis, is related to the substantia grisea in three ways: transition forms of cells occur, the cells of both groups are intimately intermingled, and both cell groups are widely and diffusely distributed. The nucleus tubero-mammillaris is therefore the least highly developed of the three groups (owing to its relation to the substantia grisea), but whether it is also the most recent group cannot be decided here; it might just as well be an old and relatively stationary group, and to decide this point a longer phylogenetic series must be studied.

The relationship of these various cell groups of the hypothalamus may be summarized as follows:

1. The substantia grisea ventriculi tertii is the oldest, least highly developed, and the most diffusely distributed cell group of the hypothalamus. From it have been differentiated at least two (and probably all) of the four cell groups that lie more or less embedded in it. Certain portions of the substantia grisea appear slightly different from the rest, in that the cells are here crowded closely together. Whether any or all of the cells of the substantia grisea take part in conducting nervous impulses, or whether this group serves merely as material from which more highly differentiated cell groups are formed, is not known.

2. From the substantia grisea at least two different cell groups have arisen; these two groups of cells have developed along diverging lines. One of these two types constitutes the nuclei tuberis laterales; it is by far the youngest cell group in the hypothalamus, the first indication of its presence occurring in the lemur. The second cell group which has developed from the substantia grisea is the nucleus tubero-mammillaris; its cell type differs radically from that of the nuclei tuberis laterales, and it is a much older cell group.

3. Along the same line as the nucleus tubero-mammillaris, and to a higher degree of histological differentiation, have developed the nucleus paraventricularis and the basal optic ganglion; the nucleus paraventricularis is intermediate between the other two nuclei. From such a short phylogenetic series as that from man to the cat it is impossible to determine whether all three of these nuclei have developed independently from the substantia grisea or whether the other two nuclei have developed from the nucleus tubero-mammillaris and thus only indirectly from the substantia grisea.

4. A more extensive series of animal forms should enable us to understand such relations better; but a study of such material cannot be expected to yield satisfactory results unless the different cell groups be distinguished and unless the question of the relationship as expressed by the cell type be borne in mind.

5. Valuable results may be expected also from a study of the histogenesis of these various cell groups as revealed in the later stages of development of the human brain; little, however, is to be expected from such material unless it be fixed and stained with reference to the demonstration of cell structure in the nervous system, and the methods usually employed are not well adapted to this purpose.

Conclusion.

I have described with the aid of illustrations the location and extent of the basal optic ganglion and nuclei tuberis laterales in four forms of mammals, and have shown their relations to the surrounding cell groups of the hypothalamus; moreover the cell types of these two cell groups have been shown to differ radically, and the differences in cell character have been pointed out through which one can readily and accurately distinguish each of these two cell groups from those which surround it. Accordingly the principal purpose of this study has been accomplished, namely, to prepare a foundation of such a character as to make further study possible. It is now possible to study in the same manner neighboring portions of the telencephalon, or to extend with relative ease the present study of the hypothalamus through a much longer phylogenetic series than the critical nature of this study has permitted; the relations of the various cell groups of the hypothalamus can be studied also from the standpoint of histogenesis; or the nature of the cell processes and the character of the nerve endings around the cells of each group may be determined. But the greatest use of this study is that it makes possible intelligent experimental investigation of the hypothalamus. Experimental workers have been inclined to pass over differences in cell character and to make little or no attempt to correlate cell function with cell character, and fail to clearly recognize a fact to which I have, in a previous article, called attention in the following words: "The histological character of a nerve cell is an indication of its function. Differences in connections with portions of the organism which differ merely in spatial relations do not involve a difference in the character of the nerve cells, but are associated merely with the *location* of the nerve cell; for instance, arm and leg muscles, flexors and extensors are all innervated by the same type of cell, although such differences in peripheral connections correspond to the differences in the position of the corresponding nerve cells." It is therefore evident that experimental work which determines the connections of various portions of a given region with different portions of the organism, without taking into consideration differences of cell character, fails to distinguish between differences of connection dependent merely upon *spatial* differences and those differences of connection which involve differences in *cell activity,* such cell activity being indicated, not only in the nervous system but in all portions of the entire organism,

by a definite type of cell character. That these two aspects of the function of the nervous system might be successfully studied in the hypothalamus by the use of experimental methods has been the controlling factor in determining the nature of this article.

But in addition to preparing a foundation for experimental work an attempt has been made to partially analyze the different elements involved in the histological complex of each cell type and to note in homologous cell groups of various animals what elements of cell character are constant; moreover in different cell groups of the same animal those elements of the entire complex of cell character which are common to the cells of two or more groups have been noted, and by this means an attempt has been made to form a provisional, although crude, idea of the degree of functional relationship among the different cell groups. At first sight such an attempt might appear premature, or it might even seem as though the task of the histologist were finished when he had pointed out the existence and location of the various cell groups, and that the determination of the functional relations of different cell groups might be safely left to the experimental worker. Such a conclusion, however, is not justified. Many regions of the brain are so complicated as to make the results of experimental investigation extremely vague, and in more suitable regions it is only under fortunate conditions that we are informed of the functional relations of a cell group except that it plays some unknown part in a complex mechanism underlying a complex function. In solving the relations of the different components of the various mechanisms of the nervous system histology must play an important and perhaps the principal part, since in the nervous system, as in the rest of the organism, it enables us to locate and to correctly state the function of every cell group of one definite cell type, if the function of this cell type has in other cell groups been previously clearly shown; that, however, it is not self-sufficient is evident.

But the neuro-histologist has a much more difficult task than that of interpreting in a general way the differences and similarities of cell character in different cell types. The cell types of certain cell groups resemble one another through possessing certain features of cell character common to all, and on the other hand differ in respect to other features of cell character; that such similarities and differences of cell type are an indication of corresponding similarities and differences of function I have already clearly shown in two cases. I have shown (Am. Jour. Anat., 1913) that although the three different types of muscle are

supplied by three distinct types of nerve cells (p. 2), these three types of nerve cells possess a fundamental similarity of cell character; accordingly the cell type varies as the cell function. In the second place I have shown (Anat. Rec., 1913) that all cells supplying striated muscle, whether directly (anterior horn cells, etc.) or more or less indirectly (large pyramidal cells, cells of Deiters' nucleus, etc.) possess certain fundamental features of cell character in common. This fundamental character makes its appearance in the first cell of any efferent chain which is set aside for the innervation of striated muscle and is present in all cells of such a series, however many neurones may intervene between the cell in question and the striated muscle fiber; on the other hand the cells in such a voluntary motor chain differ in relation to their position in the chain. It is thus evident that the particular group of elements of cell type which corresponds to the motor function of the cell may be distinguished from other elements of cell type which must correspond to the other known or unknown influences. The feature of cell character which corresponds to motor function is the arrangement of Nissl substance in relatively coarse, discrete bodies; while the large size (which is usually supposed to be common to motor cells) is not directly related to the motor function, but is an element of cell character which is probably (as stated previously) an indication of the extensive connections of the cell, in that such a large cell receives impulses from (sphere of reception) or sends impulses to (sphere of influence) a large territory.

Accordingly each type of nerve cell should be regarded not as distinct from all other types, but as the result of different influences (due to the various relations of the nerve cell to other neurones and to the other portions of the organism); when so viewed the manifold variations of cell type, including cells of the most diverse types, as well as those of extremely similar types, do not appear to offer insuperable difficulties, but on the contrary these confusing relations of cell types will enable us eventually to work out the details of various nervous mechanisms. After the simultaneous analysis, by the aid of many methods, of the histological characteristics and the functional relations of different types of cells, and after the recognition of the result of any given functional relation upon the histological character of the cell, the neurohistologist will be able to take a further step. He will not only determine one portion of the functional relation through the presence of certain features of cell character (which is already possible in the case

of various types of motor cells), *but he will actually reconstruct the greater portion of the entire complex of cell function upon the basis of the presence in the cell of certain groups of histological characters the meaning of each of which has been determined independently in different cells.* A beginning has already been made in that we are able to dissociate in motor cells the characteristic structure (corresponding to the motor activity) and the cell size (corresponding to the spheres of influence and reception of the cell); these two dissociated elements of cell character may be employed independently in examining any type of cell in the entire nervous system. Such results can be accomplished only through work which demands the exercise of the greatest critical ability, but that they will be attained I am firmly convinced.

It is evident that no such results are yet possible in the case of the hypothalamus, since no information is available concerning the functions of any of its cell groups; I have been compelled therefore to draw very general conclusions as to the nearness of functional relationship between different cell groups, since these conclusions could at present be based merely upon greater or lesser resemblance of cell type. One conclusion as to the function of these cell groups is, however, possible. The basal optic ganglion, the nuclei tuberis laterales, the nucleus paraventricularis hypothalami and the nucleus tubero-mammillaris are composed of cells whose histological character indicates that they are not efferent, but are concerned in receiving and correlating incoming impulses; these cells do not possess the relatively large, discrete Nissl bodies characteristic of efferent cells. Moreover (as suggested by Dr. Donaldson) the small size of such cells as those of the nuclei tuberis laterales would seem to indicate that the connections of these cells were less extensive than those of the cells of the other three nuclei. But now that these various cell groups have been described experimental workers will be in a position to attack the problems involving the connections and general functional significance of each of these cell groups, realizing that differences of cell type in different cell groups cannot be ignored, since such differences, as in every portion of the organism, correspond to differences in cell function; we may then expect results in this region upon which may be based in turn the constructive neuro-histology outlined above.

To those who prefer to employ several different histological methods I shall point out the fact that the Nissl method as employed by me brings out very clearly the differences and similarities of cell type, and

accordingly should with the aid of experimental work and of other histological methods suffice to give much valuable knowledge as to the real relations involved in any nervous mechanism. Every method of studying the nervous system has its advantages, and I have employed the Nissl method merely because of all methods it is the most valuable in giving a complete picture of the cell groups of the entire nervous system. To this peculiar advantage of this method, through which we can compare the histological character of all cell groups of the nervous system, I should like to direct especial attention. Such a complete picture of the cell groups of the nervous system would seem to offer a most favorable ground-work for assimilating to itself isolated facts observed by means of all other methods of studying the nervous system; without other methods (histological, experimental, etc.) it is of course of little value. (See last paragraph of introduction, p. 3.)

In my opinion the demands of such work are so exacting that each investigator who attempts to gain a picture of the cell groups of a large portion of the nervous system should confine himself, at least for the most part, to one method, and of all methods that of Nissl shows the cell structure in the clearest manner. It is not isolated cytological details obtained by many methods, nor is it the proof or disproof of the actual existence in the living cell of certain features of cell structure that will be of most importance in the above outlined constructive neuro-histology, but a thorough familiarity with the location, extent and cell type of the different cell groups of practically the entire nervous system, together with a most critical appreciation of the differences, similarities and transitions of cell type of all these cell groups; without such broad knowledge of the various cell groups, which must of course assimilate to itself isolated facts regarding the function and the connections of various cell groups directly and indirectly with one another, and facts regarding the number, character, and mode of termination of the cell processes of various cell types, without such a comprehensive knowledge upon which to build we could not hope to penetrate far into the exact relations of the individual neurones of the nervous system.

Literature.

The literature on the cell groups of the hypothalamus has been of practically no assistance to me. In the first place I did not read it until I had worked out these groups in the human brain, and upon

reading it found no reason for modifying my conception of this region. In the second place some of the articles are concerned with animal forms so far removed from those upon which I have worked that the recognition of homologous groups is by no means certain. Finally the descriptions of cell groups are often so inadequate and so little attention is given to the differences in cell type as to make the literature, except in rare cases, almost unintelligible; this is true especially in those articles which are concerned with the brain of man and the higher mammals. Accordingly the results of other workers on the cell groups of the hypothalamus have not been incorporated to any great extent into the body of this article, but are here appended for the sake of completeness; to treat the greater portion of the literature otherwise would render the subject of this article needlessly obscure. The following consideration of the literature is given for the benefit of those who wish to make a careful study of the region in question; accordingly it appears advisable not to give an abstract of the various articles, since the complete accounts must be read by those for whom the following consideration is intended. On the contrary I shall for the most part confine myself to a consideration of certain points, showing wherein certain accounts are correct and wherein erroneous, and wherein some descriptions are altogether unintelligible.

The description of the cell groups of the hypothalamus contained in my monograph on the human diencephalon has been referred to in numerous places in the text and a further reference is unnecessary.

In Stricker's Manual of Histology (American translation) Meynert gives a brief but fairly clear description of the basal optic ganglion; on p. 688 he says: "At the lateral border of the tuber cinereum lies the inferior optic ganglion, which is 1.5 mm. broad, and contains spindle-shaped cells 30 μ in length and 15 μ in breadth. It begins just above the optic commissure and stretches along immediately over the tractus opticus as far as the posterior border of the tuber cinereum, a distance of more than a centimeter. I regard, with Luys, this optic ganglion as a part of the tuber cinereum, because it projects downwards, in company with the latter, into the lamina cinerea, beyond the surface of the lamina perforata anterior, of which J. Wagner considers it to be a part, and because it extends farther backward than the latter. Like the tractus itself, however, it certainly follows the inner border of the anterior perf. space. On profile sections (Fig. 270, II′) this ganglion has a sickle-like shape, the concavity looking forward. According to Luys, the two ganglia touch at the median line, a fact which I have not been able to verify, etc." From this description and from a study of Fig. 268 it is clear that Meynert had in mind a cell group which has much in common with that described under the same name

in the present article. The exact extent is, however, not clear, and we have no assurance that he distinguished between this cell group and the nucleus tubero-mammillaris, or that he included all portions of the basal optic ganglion. Moreover he was unable to observe the union of the ganglia of opposite sides, a fact which makes it almost certain that he failed to include the medial portion of each ganglion.

When we attempt to understand the article of von Lenhossék, in which he divides, in man, the basal optic ganglion of Meynert into a nucleus supra-opticus and two nuclei tuberis, we are confronted with an impossible task. We are informed that all three nuclei are composed of small, spindle-shaped, multipolar nerve cells, as well as neuroglia; this is a most disturbing statement and renders it absolutely impossible to form any idea as to what cell groups the author had in mind. For by no means can the cells of the basal optic ganglion be termed small, since they measure up to 35 μ in diameter, and compared with the cells of the nuclei tuberis and the substantia grisea their large size is most evident (Fig. 37). Accordingly the word "small" would seem to make it certain that Lenhossék's nucleus supraopticus cannot be a portion of Meynert's basal optic ganglion; and yet after Meynert's description and illustrations it would seem remarkable for anyone to overlook such a prominent cell group as the oral portion of the basal optic ganglion. Again we are informed that the nucleus anterior of the tuber cinereum is the largest of all three nuclei (nucleus supra-opticus and the anterior and postero-lateral nuclei of the tuber) "*und bildet eigentlich den Hauptbestandteil des Tuber.*" and that apparently it reaches the median line. What can this mean? Can the "small" cells of this anterior nucleus be the large cells of the nucleus tubero-mammillaris, or is this nucleus a portion of the substantia grisea? One is almost tempted to infer from Lenhossék's description that his three portions of Meynert's basal optic ganglion are a complex of what I have described as the basal optic ganglion and portions of the nucleus tubero-mammillaris, all of which are composed of large cells, and that the cells of the substantia grisea he may possibly have considered neuroglia; since he employed the Weigert stain such a mistake is by no means improbable. But just what the three nuclei of Lenhossék represent is absolutely impossible to determine.

Kölliker's description of the nuclei tuberis and the basal optic ganglion I have in a previous article termed *vortrefflich;* this implies a uniform excellence which this description by no means possesses. It were more fitting to term Kölliker's account of these nuclei "remarkable," for it is remarkable as to insight into this complicated region, and at the same time remarkable for the contradictions, incorrectly labeled figures, and other faults which detract from its value. Only to one who has made a thorough study of this region is the difference apparent between the unintelligible description of von Lenhossék and the essential excellence of that of Kölliker, and from 1896 until 1910 no one has made himself sufficiently familiar with this region to realize the many excellent points in Kölliker's work. The real contributions of Kölliker are as follows:

Es müssen Nuclei tuberis von den Nuclei supraoptici unterschieden werden (p. 602)...*Die Nuclei tuberis kommen mehr in den medialen Gegenden vor, besitzen kleine Nervenzellen, etc.* (p. 603)...*Die Nuclei supraoptici haben grössere Zellen, etc.* (p. 603). Moreover Figs. 704 and 705 are correctly labeled and entirely intelligible. Fig. 702 shows the nuclei tuberis laterales excellently, but unfortunately they are termed "ganglia optica basalia"; on p. 599 these groups are correctly termed nuclei tuberis, while on p. 519 they are incorrectly termed (in text) "ganglia optica basalia." This uncorrected error in Fig. 702 is unfortunately characteristic of the inconsistent nature of Kölliker's description. But in Fig. 631 we meet a further difficulty, since the cell mass of the tuber which in Fig. 631 (rabbit) is termed "Ganglion opticum basale" is stated on p. 603 to represent the "Ganglia tuberis"; in reality this cell mass is simply a portion of the substantia grisea and is not the nuclei tuberis laterales (which are shown in Figs. 702, G. o. b., and 705, G. t.). On p. 599 he has incorrectly stated that the nuclei tuberis are continued more or less definitely into two of the groups of the corpus mammillare, nucleus intercalatus (or possibly a separated portion of the medial nucleus as discussed in my monograph on the diencephalon) and the nucleus tubero-mammillaris; this proves beyond doubt that Kölliker's nuclei tuberis are to be regarded as topographical groups rather than determined by a definite cell character. On the other hand he has confused a portion of the nucleus tubero-mammillaris with the basal optic ganglion; on p. 600 he says: *Dieser Kern ist schon in der Fig. 703 in der Grenzlage zwischen dem Tractus opticus, dem Reste des Pes pedunculi und dem Nucleus Tuberis lateralis in den ersten Anfängen vorhanden und zwar wie in der Linsenkernschlinge drin, wird aber nach vorn immer grösser, etc.* Accordingly Kölliker has included portions of the nucleus tubero-mammillaris with the nuclei tuberis on the one hand, and on the other with the basal optic ganglion. The vacant space surrounding the third ventricle in his figures raises the question as to how he regarded the substantia grisea of the third ventricle; its relations to the other nuclei he has failed to point out, and in how far he confused this cell mass with the nuclei tuberis we cannot determine, except in Fig. 631 in case of the rabbit, where this error is apparent; this cell group of the rabbit is the substantia grisea and does not correspond to the nuclei tuberis as shown in his figures of man. In conclusion, Kölliker's description and figures are often very faulty, but on the other hand in his figures may be recognized in many cases cell groups correctly represented.

Cajal (pp. 756-757) describes in rodents a cell group under the name *ganglio peri-kiasmático o tangencial* which without doubt is homologous with the basal optic ganglion of higher mammals. He is in doubt as to whether it corresponds to the supraoptic nucleus of Lenhossék and the supraoptic complex of Kölliker. As previously explained it is impossible to identify the supraoptic nucleus of Lenhossék, especially since he says that it is composed of "small" cells; the description of Cajal ás well as his excellent illustration (Fig. 640) shows that the *ganglio peri-kiasmático* is

composed of large cells. Cajal further states that there is a great difference in form, position and extent between this ganglion of rodents and the above human centers. While I have not yet studied the basal optic ganglion in rodents I am strongly of the opinion that this ganglion in rodents does not differ essentially either in form, position or extent from the basal optic ganglion in man; I base this conclusion on the constancy of this ganglion from man to the cat, and upon Cajal's description and illustration. There is no difficulty in recognizing that the centers, which Cajal describes in the tuber under the names of anterior, posterior and superior nuclei of the tuber, are portions of the substantia grisea and have nothing to do with the nuclei tuberis laterales of man and macacus; the difference in location of these three nuclei and the fact that there is every reason to believe that the nuclei laterales are not present in the rodents (appearing first in the lemur) renders confusion impossible. Under the name *núcleo subventricular* Cajal describes (p. 731) a cell column which is beyond doubt homologous with the nucleus paraventricularis hypothalami, which I have described in man and the higher mammals; Cajal's description and illustration (Fig. 604, T) place this fact beyond the possibility of a doubt. Accordingly Cajal's description of the hypothalamus enables us to recognize positively two characteristic cell groups in rodents one of which is homologous with the basal optic ganglion and the other with the nucleus paraventricularis hypothalami of higher animals. Concerning the complex of the nucleus tubero-mammillaris we are left in doubt.

The presence of the basal optic ganglion and the nucleus paraventricularis is certain not only in rodents but even in the marsupials, as is seen from Ziehen's description of the brain of Pseudochirus peregrinus. In describing Fig. 28 he says (p. 713): *Sehr schön ausgeprägt ist beiderseits das Ganglion opticum basale (nucleus supraopticus). Rechts sendet es einen langgestreckten Ausläufer in das Pedamentum laterale. Ingesammt erstreckt es sich über 1.3 mm. in sagittaler Richtung. Seine Zellen messen 21 μ. Frontalwärts reicht es noch ein wenig über den vorderen Chiasmarand hinaus. Einen Zerfall in mehrere Zellgruppen, wie ihn Lenhossék und Kölliker bei dem Menschen beschrieben haben, vermöchte ich nicht sicher nachzuweisen.* On p. 714 in describing this same section (Fig. 28) Ziehen says: *In der grauen Masse zu beiden Seiten des 3 Ventrikels kann man—in der Reihenfolge von untcn nach oben—folgende Theile unterscheiden. Unmittelbar oberhalb des Chiasmas folgt der kleinzellige Nucleus tuberis* (evidently the substantia grisea), *auf diesen ein gross-zelliger lateraler Kern, in welchem der Fornixsäule eingebettet ist* (a portion of my nucleus tubero-mammillaris), *und ein eben so grosszelliger medialer Kern, welcher der Ventrikelwand unmittelbar anliegt.* This latter nucleus is evidently homologous with the nucleus paraventricularis hypothalami, and I thoroughly agree with Ziehen when he continues as follows: *Bei der sehr starken Ausprägung des letzeren war ich sehr erstaunt, eine ähnliche Bildung bei anderen Säugern nirgends beschrieben zu finden. Ich will den Kern einstweilen als Nucleus subcommissuralis bezeichnen.* Ziehen's

illustrations unfortunately show almost nothing of the various cell groups, but his concise description is most valuable.

Worthy of special notice is the valuable contribution of Friedemann entitled *Die Cytoarchitektonik des Zwischenhirns der Cercopitheken mit besonderer Berücksichtigung des Thalamus opticus.* As the title indicates more attention is paid to the thalamus than to the hypothalamus, although both the pars mammillaris and the pars optica are by no means neglected. In this article Friedemann takes into consideration my monograph on the human diencephalon. To consider intelligently Friedemann's account of the cell groups of the hypothalamus it is necessary to realize that his chief purpose is to subdivide this region into topographical cell groups, which are not necessarily composed exclusively of one type of cell, but may represent complex centers formed by the overlapping of several primary nuclei; on the other hand he has occasionally divided a cell mass, composed of cells of the same type, into subgroups whenever factors other than cell character (such as number and grouping of cells) would permit. In this he has consistently endeavored to give us a topographical subdivision into as many areas as may possibly be distinguished in cell preparations. It is accordingly evident that my cell groups (primary nuclei) have been set aside in virtue of the possession of one type of cell which corresponds to some known or unknown cell function or functions and that the topographical value of my work is primarily concerned with the location and distribution of such a single cell type; and on the other hand it is evident that Friedemann's subdivision, not being confined to this one criterion of cell character, results in a much more minute subdivision which is of great value in exact orientation, and that his cell groups may represent primary nuclei, portions of such nuclei, or complex nuclei, according to the criteria employed in the establishment of each cell group. Apparently Friedemann has not grasped this fundamental difference in our aims, since (p. 312) he says: *So wichtig auch u. a. die von Malone festgestellte Tatsache ist, dass im Thalamus opticus keine Zellen vom motorischen Typus vorkommen, so sehr wir auch in vielen Einzelheiten mit diesem Autor übereinstimmen, als topographisches Einteilungsprinzip können wir seine Methode nicht anerkennen.* It is certainly my earnest desire that no one should consider the method I have employed as a *topographisches Einteilungsprinzip,* since I myself have never so considered it, and had supposed that I had made this fact evident. But Friedemann's work is something more than a pure topographical subdivision, since he has informed us as to whether a cell group has been recognized on account of its cell type, or whether it is differentiated from the surrounding cells on the basis of other criteria; in other words he has, in giving us this minute and most valuable topographical subdivision, not lost sight of the distribution of the various cell types. The fact that Friedemann and myself have subdivided the diencephalon from different points of view is a fortunate circumstance, and the difference in results is to be expected and welcomed. Other subdivisions from other standpoints are desirable, but it is essential that we be accurately informed

just what criteria have been employed in setting aside each cell group; and moreover we should carefully distinguish between such cell groups of different authors as are identical and such as do not entirely correspond.

Taking up the various cell groups of the hypothalamus, Friedemann describes the nucleus intercalatus corporis mammillaris and the nucleus paraventricularis just as I had found them in man, and he adopts my names for them. He also adopts my name "nucleus mammillo-infundibularis"; I have previously in this article pointed out that this name must be changed, and have adopted instead that of nucleus "tubero-mammillaris." But it is not clear to me that Friedemann has included all the cells in this group which I have assigned to it; unfortunately the illustrations (photographs) are of little value in showing the distribution of each cell type. It is certain that his nucleus posterior pedamenti lateralis (Fig. 9, Plp) is a portion of my nucleus tubero-mammillaris; moreover Friedemann has called attention to the fact (p. 367) that his lamina grisea separans (Fig. 9, lgs) is a portion of this same nucleus. Such subdivisions are of course desirable for their topographical value, but the common cell character should be kept in mind. In considering the basal optic ganglion Friedemann has fallen into the same error that I did in my monograph on the diencephalon, and for the same reason, since both of us were not primarily interested in the telencephalon; this error consists in considering merely the cell mass which follows the oro-lateral border of the optic tract as constituting this ganglion. It is certain that to the basal optic ganglion of cercopithecus must be added Friedemann's "nucleus anterior pedamenti lateralis" (p. 370 and Fig. 11, Pla) as well as his "stratum supraopticum" (p. 369 and Fig. 9, Sso.). That these two cell groups belong to the basal optic ganglion is clear both from the descriptions and illustrations. It is unfortunate that neither the cross sections nor the horizontal sections illustrated give the region just caudal to the optic chiasm. Friedemann's cross sections may be best compared with my Series D of man (Figs. 11 to 18) since the plane of section is similar; in comparing these two series it is evident that the most oral section (Fig. 11) of Friedemann stops short of a most important region of the basal optic ganglion. Again his first horizontal section (Fig. 12) likewise fails to give this region near the optic chiasm. (The omission of this region is only natural, since Friedemann's article deals primarily with the diencephalon.) Accordingly I see no reason to believe that the basal optic ganglion in cercopithecus is essentially different from that in other animals from man to the marsupials.

In Friedemann's description of cercopithecus I am unable to find any cell groups which would correspond to the nuclei tuberis laterales, and unfortunately the illustrations are of such a nature (photographs) as not to reveal the presence of such groups. It is not probable that the nuclei tuberis laterales are wanting in cercopithecus, since they are present in macacus and are indicated even in the lemur; their presence, if indeed they occur in cercopithecus, might easily be overlooked unless one had seen them in man, where these nests of cells are very definite. The fact, which

Friedemann himself has pointed out (p. 367-8), should be most carefully noted: Friedemann's nuclei of the tuber cinereum are different portions of the substantia grisea; he calls attention moreover to the fact (p. 367) that the substantia grisea has been divided into these nuclei rather on account of topographical relations and differences in the crowding together of cells than on account of differences in cell form. Accordingly these topographical cell groups of the substantia grisea must not be confused with the nuclei tuberis laterales, since the latter are composed of cells of another type.

Bibliography.

Cajal, S. R. y: Textura del sistema nervioso, etc., 1904, vol. 2.

Forel, A.: Beiträge zur Kenntnis des Thalamus opticus, etc. Gesammelte hirnanatomische Abhandlungen, 1872, pp. 17-43. (Published originally in Bd. 66 der Sitzb. der k. Akad. d. Wissensch. in Wien, dritte Abteilung, Juni.)

Friedemann, M.: Die Cytoarchitektonik des Zwischenhirns der Cercopitheken, etc. Jl. f. Psychologie u. Neurol., 1911, XVIII, Ergänzungsheft 2.

Ganser, L.: Vergleichende anatomische Studien über das Gehirn des Maulwurfs; Morpholog. Jahrbuch, 1882, VII.

Kölliker, A.: Handbuch der Gewebelehre, 1896, II.

von Lenhossék, M.: Beobachtungen am Gehirn des Menschen, Anat. Anz., 1887, II, Nr. 14.

Malone, E.: Über die Kerne des menschlichen Diencephalon. Aus dem Anhang zu den Abhandlungen der königl. preuss. Akad. d. Wissensch., 1910.

Observations concerning the comparative anatomy of the diencephalon. Anat. Rec., 1912, VI, No. 7.

Recognition of members of the somatic motor chain of nerve cells, etc. Anat. Rec., 1913, VII, No. 3.

The nucleus cardiacus nervi vagi, etc. Am. Jour. Anat., 1913, XV, No. 1.

Meynert, Th.: The brain of mammals. Stricker's manual of histology (American translation), 1872.

Ziehen, Th.: Das Centralnervensystem der Monotremen und Marsupialier. Teil 2, erster Abschnitt. From Semon's Forschungsreisen, III.

Explanation of Illustrations.

Figs. 1 to 35 and 1A to 35A have been prepared in the following manner: The entire section was in each case projected at a magnification of ten diameters, and the outlines together with as many details as possible were drawn in pencil; even bloodvessels, tears in the section, particles of detritus, etc., were drawn in so as to serve the purpose of orientation. Under the microscope at the same magnification (ten diameters) the drawing was completed, with the occasional aid of higher magnification. (Of course the drawings were not begun until I had a clear idea of the location, extent, cell character, and relations of the various cell groups.) This completed drawing is not used for publication but serves as the basis for two others. In the first place an outline drawing is made (by tracing) and the various structures labeled (Figs. 1A to 35A); in these drawings a rectangular area is indicated which contains the region in which we are interested. A second series of drawings (Figs. 1 to 35) are traced from that portion of the original included within the rectangular area, and the details filled in, under control of the microscope. Finally these two series of drawings have been reproduced in parallel columns; in order to do this the outline drawings have been more greatly reduced in size than the detailed drawings, the resulting magnification being indicated in the explanation of each plate. Figs. 1 to 18 have been so much reduced that they should be examined with the aid of a hand lens; the cells of the nuclei tuberis laterales are especially difficult to recognize without such aid.

It is important to understand just what these drawings are intended to illustrate. The outline series (Figs. 1A to 35A) needs no explanation, except the statement that the size and relations of the structures shown have been accurately reproduced. In the other series (Figs. 1 to 35) the distribution of each cell group is accurately shown, each being indicated by one type of cell which may be distinguished in all drawings from the cells of all other cell groups; thus different cell groups may be distinguished when their cells are intermingled, and it is thereby possible to reproduce the actual extent of each cell type without resorting to an arbitrary boundary. On the other hand in order to indicate differences in cell type it has been necessary to make the cells much larger than they appear at such a low magnification, and this in turn involves a reduction in the number of cells. However, the relative density of each cell mass in its various portions is shown, and the relative size of different cell types has been maintained, although this difference in size has in some cases been somewhat exaggerated in order to make it more obvious. For a true picture of each cell type one must study Figs. 38 to 58, in which each cell type has been reproduced exactly as it appears.

The exact cell size and distance between the cells of the nuclei tuberis laterales and the basal optic ganglion, as well as that of the surrounding cell groups, has been reproduced exactly in Figs. 36 and 37, which also show the different cell types as they appear at a relatively low magnification. These two illustrations (Figs. 36 and 37) will be explained on the pages facing them.

Figures 38 to 58 were drawn as follows:

With the aid of the camera lucida the cell outlines and as many details as possible were drawn in pencil. Then under control of the microscope the exact appearance of the cells was reproduced in water color. Each cell is to be regarded as an individual and the spatial relations of the cells in each figure do not correspond to those between the cells of the corresponding cell group in the preparations. In these figures the cells have been reproduced by combining to a certain extent different optical sections of the same cell. All cells have been drawn at a magnification of 580 diameters, and have been reproduced without reduction. Figs. 38 to 58 were all drawn from cross-sections of the brains of the various animals. In Series D of man the plane of section differs widely from that of a cross-section, and yet (without making a careful study of this point) I was unable to observe that this difference in the plane of section was correlated with any difference in the appearance of the cell types here illustrated. On the contrary I can state positively that each of the above types of cells was as characteristic in Series D as in Series AC, and that differences in the plane of section could not possibly lead to a confusion of the different cell types.

PLATE I.

Homo. Series AC.

Magnification of Figs. 1 to 4 = 5 diameters.
Magnification of Figs. 1A to 4A = 2 diameters.

● = Cells of the nucleus tubero-mammillaris (formerly known as nucleus mammillo-infundibularis).

• = Cells of the substantia grisea ventriculi tertii.

Δ = Cells of the nuclei tuberis laterales (n. t. l.). (Examine with hand lens).

○ = Cells of the ganglion opticum basale (g. o. b.).

⊙ = Cells of the corpus hypothalamicum (Luysii).

FIG. 1.

FIG. 1A.

FIG. 2.

FIG. 2A.

FIG. 3.

FIG. 3A.

FIG. 4.

FIG. 4A.

PLATE II.

HOMO. SERIES AC (CONTINUED).

Magnification of Figs. 5 to 7 = 5 diameters.
Magnification of Figs. 5A to 7A = 2 diameters.

● = Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
• = Cells of the substantia grisea ventriculi tertii.
Δ = Cells of the nuclei tuberis laterales (n. t. l.). (Examine with hand lens).
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = Cells of the corpus hypothalamicum (Luysii).

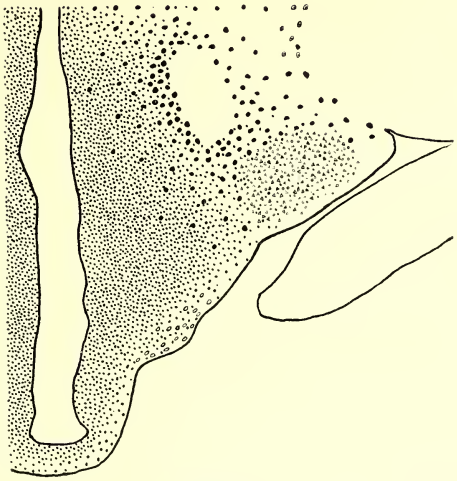


FIG. 5.

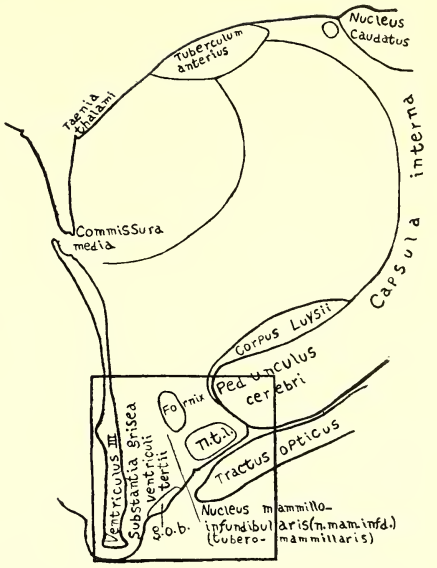


FIG. 5A.

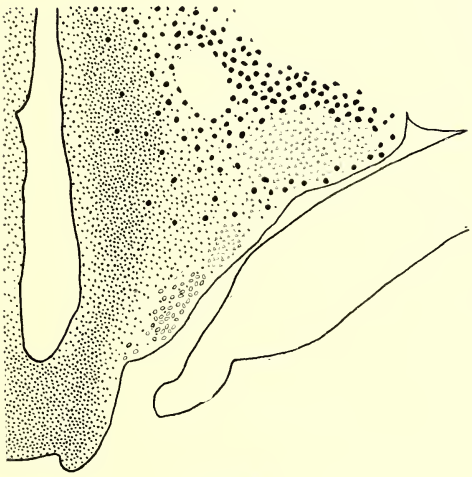


FIG. 6.

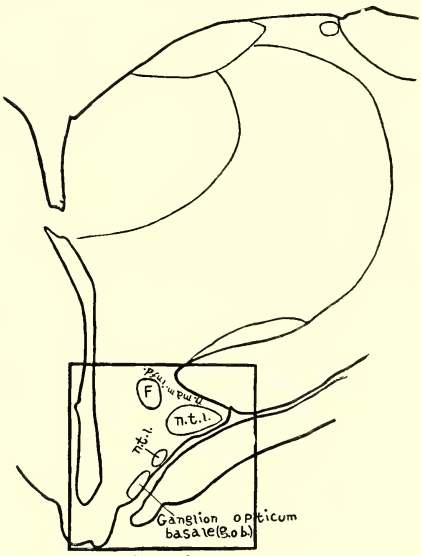


FIG. 6A.

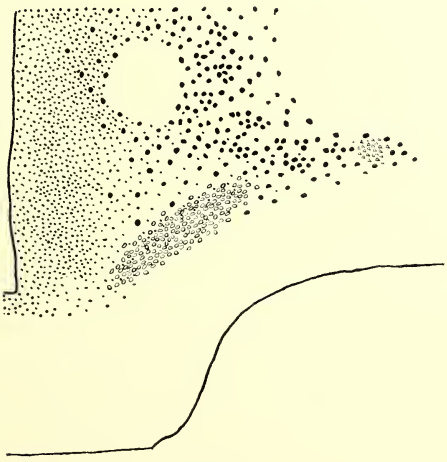


FIG. 7.

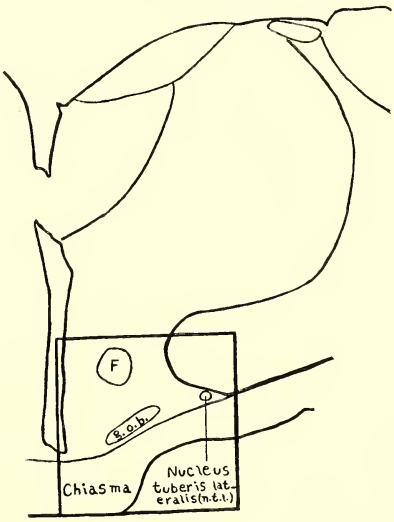


FIG. 7A.

PLATE ~~VI.~~ III

HOMO. ~~MAGNIFICATION = 580 DIAMETERS.~~

38. Cells of the ganglion opticum basale.
39. Cells of the nuclei tuberis laterales.
40. Cells of the substantia grisea ventriculi tertii.
41. Cells of the nucleus tubero-mammillaris (formerly known as nucleus mammillo-infundibularis).
42. Cells of the nucleus ansae peduncularis (also known as ganglion basale of Kölliker).
43. Cells of the nucleus paraventricularis hypothalami.

Plate III.

Homo. Series AC (concluded)

magnification of figures 8 to 10 = 5 diameters.

" " " 8A to 10A = 2 " .

= Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).

= " " " substantia grisea ventriculi tertii.

= " " " nuclei tuberis laterales (n.t.l.) (Examine with hand lens).

= " " " ganglion opticum basale (g.ob.).

= " " " nucleus ansae peduncularis (ganglion basale of Kölliker).

Note that the cells of the nucleus tubero-mammillaris and those of the nucleus paraventricularis are represented by the same type of cell; moreover the same type of cell has been employed to represent the cells of the corpus subthalamicum and those of the nucleus ansae peduncularis. It seems advisable to use one type of cell to represent cells of two different groups, when these two groups are clearly distinguishable topographically, rather than to multiply the number of symbols used, and thus make it more difficult to distinguish between them. The outline drawings make a confusion of such cell groups impossible.

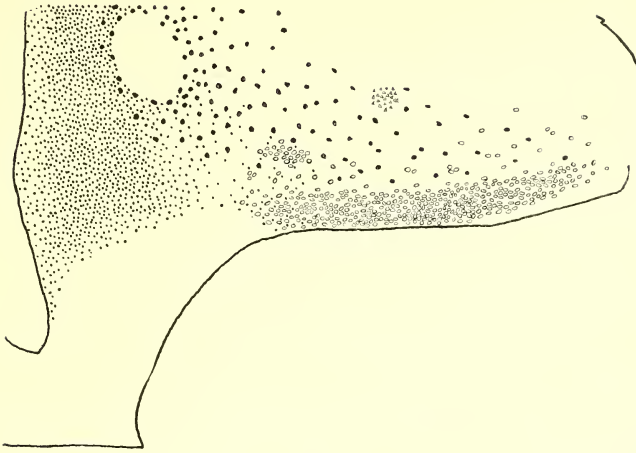


FIG. 8.

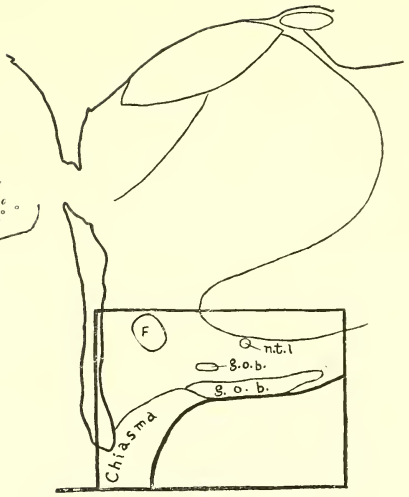


FIG. 8A.

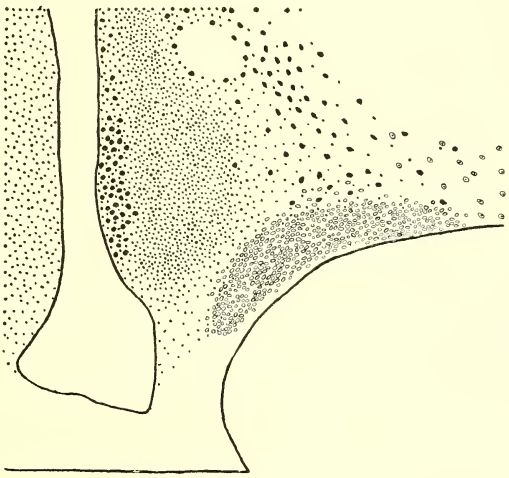


FIG. 9.

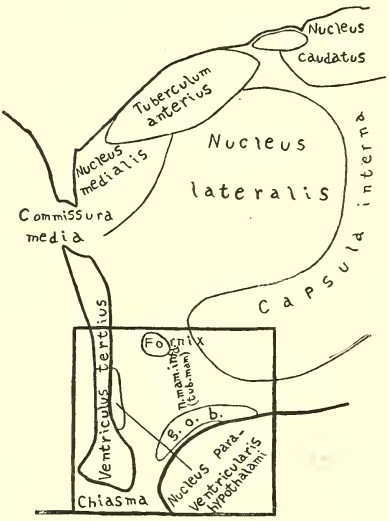


FIG. 9A.

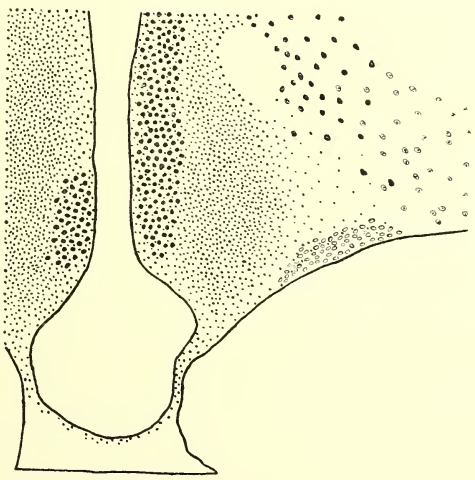


FIG. 10.

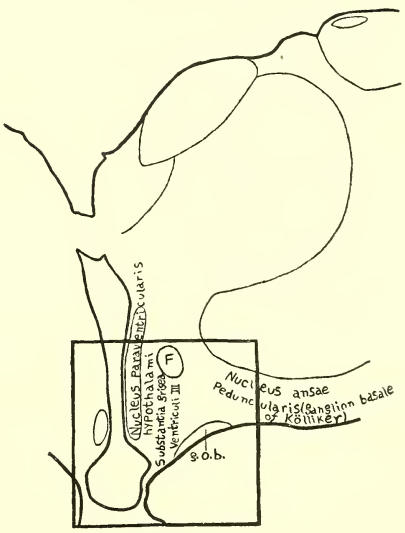


FIG. 10A.

Plate IV. Homo. Series D.

magnification of figures 11 to 14 = 5 diameters.

" " " 11A to 14A = 2 diameters.

= Cells of the nucleus tubero-mammillaris (nucleus mammilo-infundibularis).

= " " " substantia grisea ventriculi tertii.

= " " " nuclei tuberis laterales (n.t.l.) (Examine with hand lens).

= " " " ganglion opticum basale (G.O.b.).

= " " " ganglion mediale corporis mammillaris.

= " " " nucleus intercalatus corporis mammillaris.

= " " " cortex cerebri.

= " " " Globus pallidus nuclei lentiformis

" " " nucleus ansae pedunculoris.

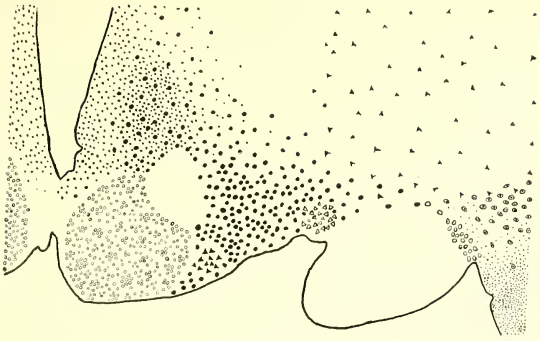


FIG. 11.

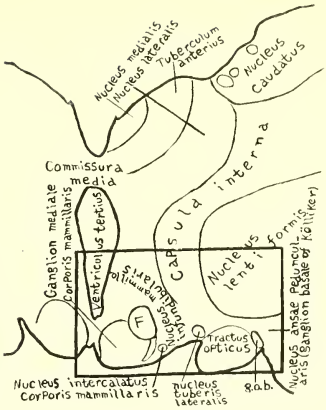


FIG. 11A.

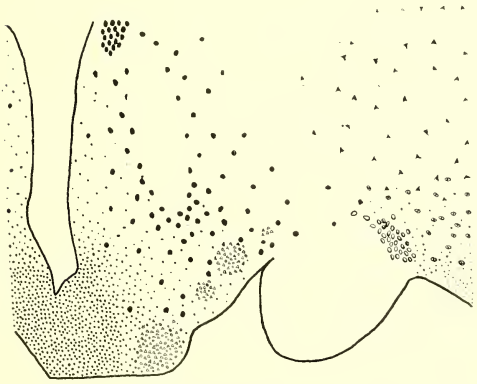


FIG. 12.

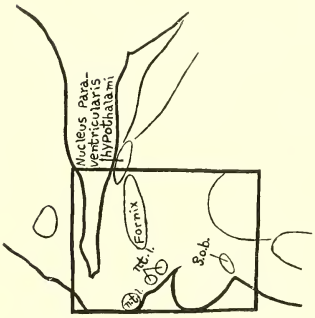


FIG. 12A.



FIG. 13.

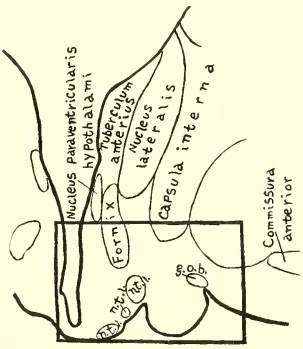


FIG. 13A.

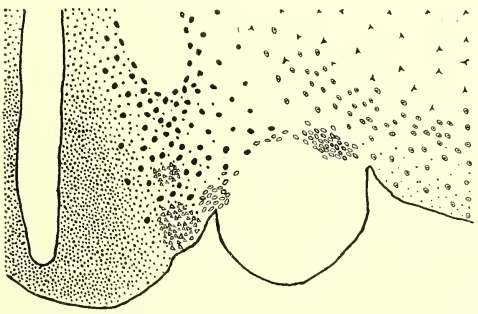


FIG. 14.

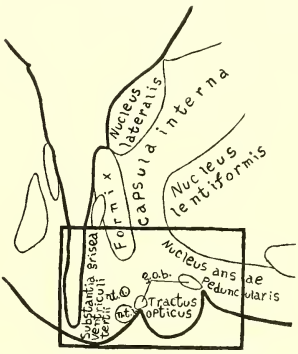


FIG. 14A.

PLATE V.

Homo. Series D (Continued).

Magnification of Figs. 15 to 18 = 5 diameters.
Magnification of Figs. 15A to 18A = 2 diameters.

● = { Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
Cells of the nucleus paraventricularis hypothalami.

• = Cells of the substantia grisea ventriculi tertii.
Δ = Cells of the nuclei tuberis laterales (n. t. l.). (Examine with hand lens).
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = Cells of the nucleus ansae peduncularis.
. = Cells of the cortex cerebri.
≻ = Cells of the globus pallidus nuclei lentiformis.

Note in Fig. 17 the closely packed group of cells of the substantia grisea situated just lateral to the ventral tip of the third ventricle (see text).

Note in Fig. 18 the cells of the basal optic ganglion crossing mid line (see text).



FIG. 15.

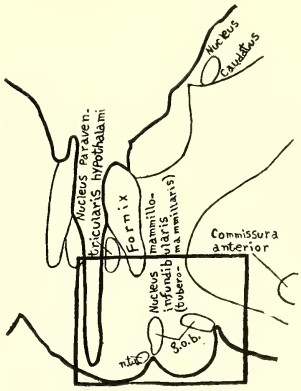


FIG. 15A.



FIG. 16.

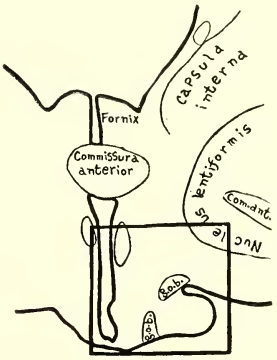


FIG. 16A.



FIG. 17.

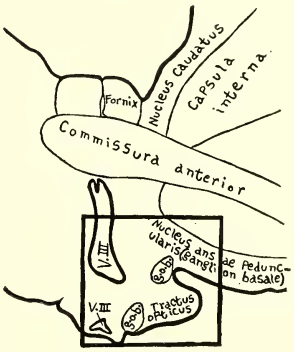


FIG. 17A.



FIG. 18.

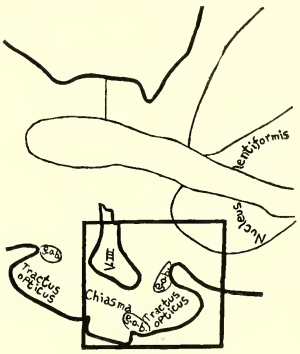


FIG. 18A.

PLATE VI.

MACACUS RHESUS. SERIES A.

Magnification of Figs. 19 to 22 = 6⅔ diameters.
Magnification of Figs. 19A to 22A = 2½ diameters.

● = Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
• = Cells of the substantia grisea ventriculi tertii.
Δ = Cells of the nuclei tuberis laterales (n. t. l.).
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = Cells of the corpus hypothalamicum (Luysii). / Cells of the nucleus ansae peduncularis.
° = Cells of the ganglion mediale corporis mammillaris.
▸ = Cells of the nucleus intercalatus corporis mammillaris.
. = Cells of the cortex cerebri.
≻ = Cells of the globus pallidus nuclei lentiformis.

Note in Fig. 22 the group of densely packed cells of the substantia grisea located just lateral to the third ventricle (see text).

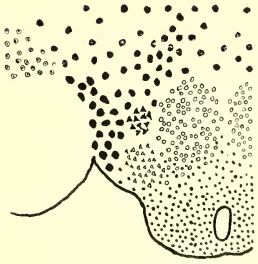


FIG. 19.

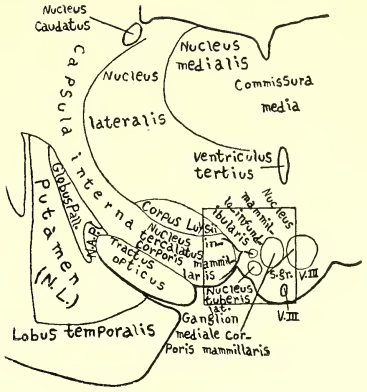


FIG. 19A.

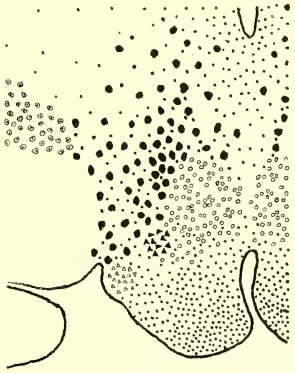


FIG. 20.

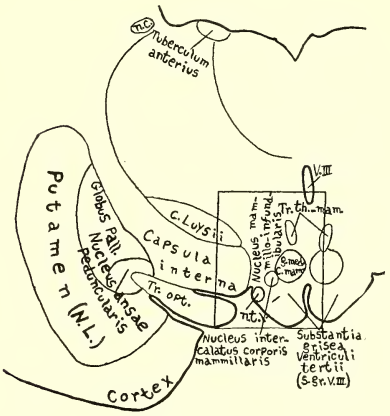


FIG. 20A.

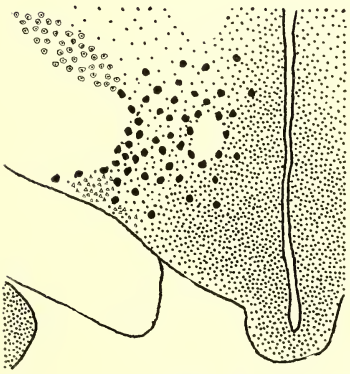


FIG. 21.

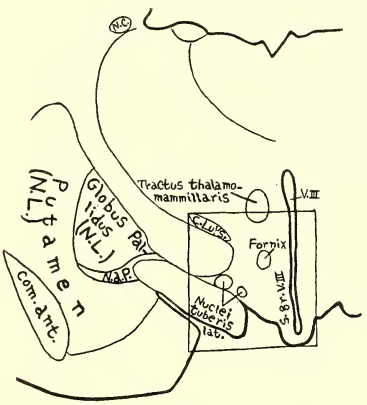


FIG. 21A.



FIG. 22.

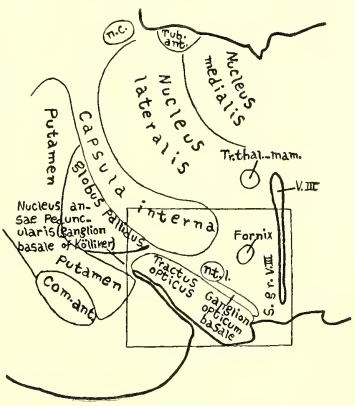


FIG. 22A.

PLATE VII.

MACACUS RHESUS. SERIES A (CONTINUED).

Magnification of Figs. 23 to 25 = 6⅔ diameters.
Magnification of Figs. 23A to 25A = 2½ diameters.

● = { Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
Cells of the nucleus paraventricularis hypothalami.

• = Cells of the substantia grisea ventriculi tertii.
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = Cells of the nucleus ansae peduncularis (ganglion basale of Kölliker).
. = Cells of the cortex cerebri.
⟩ = Cells of the globus pallidus nuclei lentiformis.

Note in Fig. 24 lateral from the third ventricle the densely packed group of cells of the substantia grisea; such masses of the substantia grisea should not be confused with the nuclei tuberis laterales.

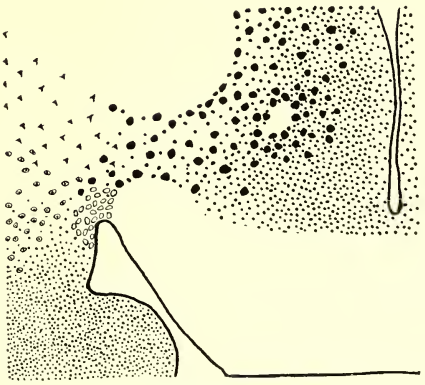


FIG. 23.

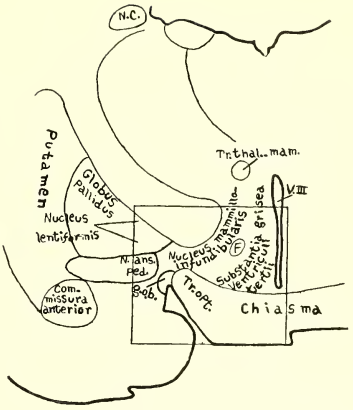


FIG. 23A.

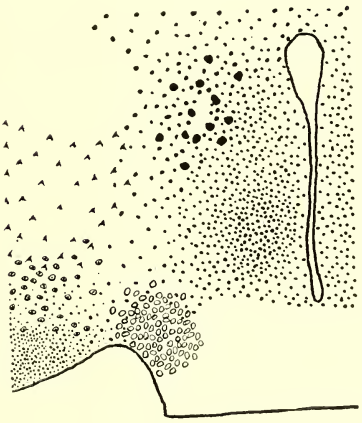


FIG. 24.

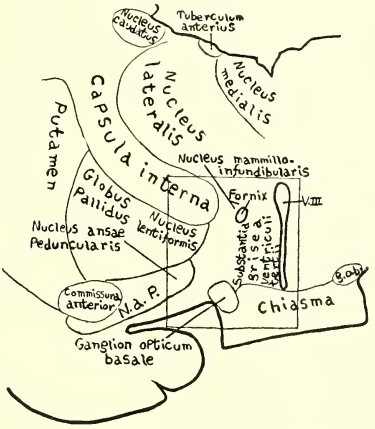


FIG. 24A.

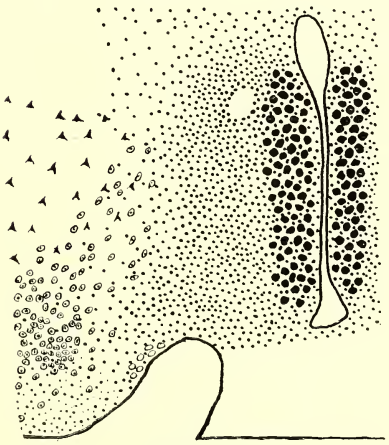


FIG. 25.

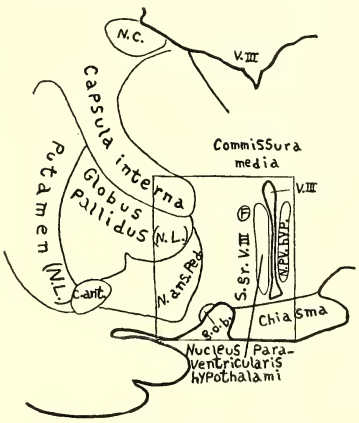


FIG. 25A.

PLATE VIII.

LEMUR RUFUS. SERIES A.

Magnification of Figs. 26 to 30 = 8⅓ diameters.
Magnification of Figs. 26A to 30A = 3⅓ diameters.

● = { Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
Cells of the nucleus paraventricularis hypothalami.

• = Cells of the substantia grisea ventriculi tertii.
○ = Cells of the ganglion opticum basale (g. o. b.).
≻ = Cells of the globus pallidus nuclei lentiformis.

Note in Fig. 27 the absence of the basal optic ganglion (see text).

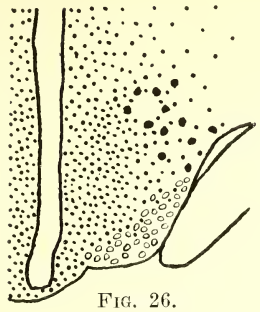


FIG. 26.

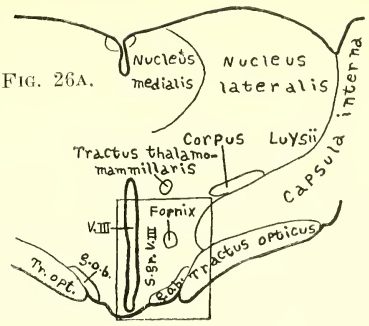


FIG. 26A.

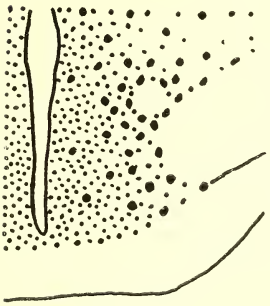


FIG. 27.

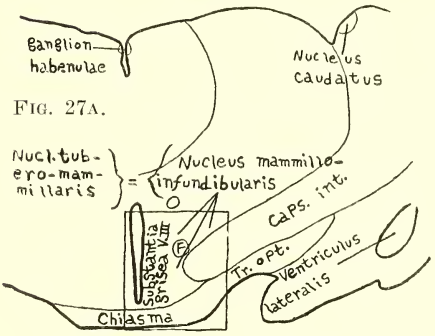


FIG. 27A.

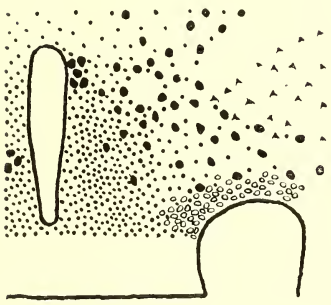


FIG. 28.

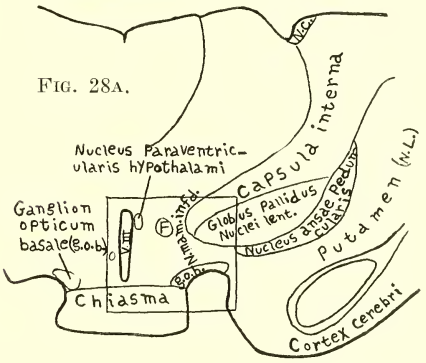


FIG. 28A.

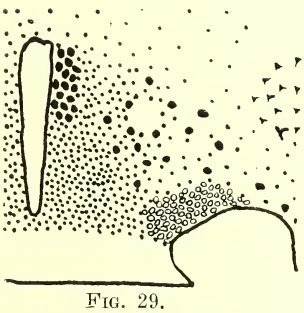


FIG. 29.

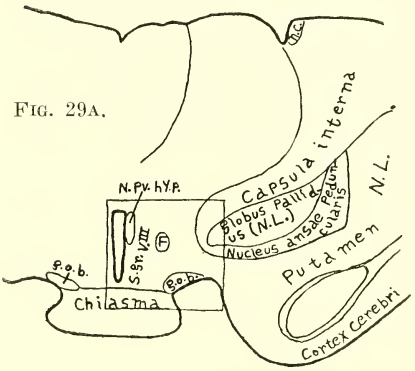


FIG. 29A.

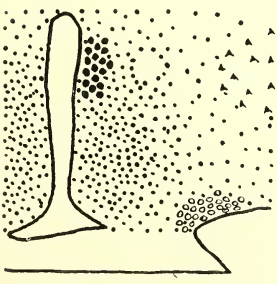


FIG. 30.

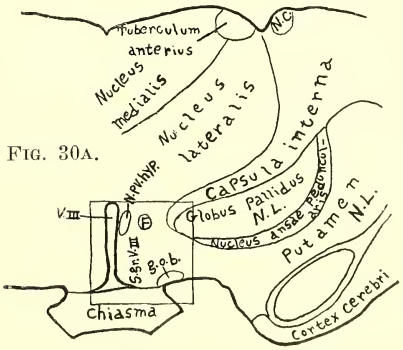


FIG. 30A.

PLATE IX.

Cat. Series C.

Magnification of Figs. 31 to 35 = 8½ diameters.
Magnification of Figs. 31A to 35A = 3⅓ diameters.

● = { Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
Cells of the nucleus paraventricularis hypothalami.

• = Cells of the substantia grisea ventriculi tertii.
○ = Cells of the ganglion opticum basale (g. o. b.).
. = Cells of the cortex cerebri.
≻ = Cells of the globus pallidus nuclei lentiformis.

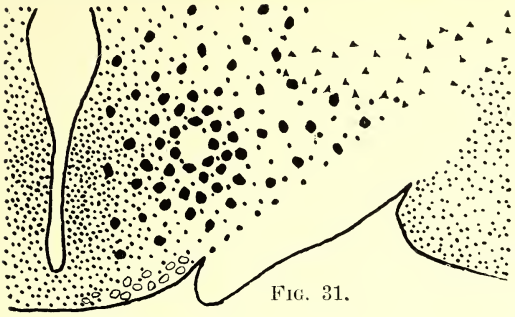


FIG. 31.

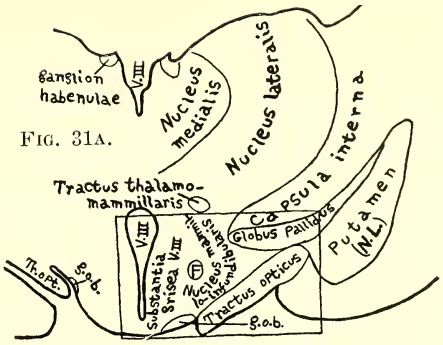


FIG. 31A.

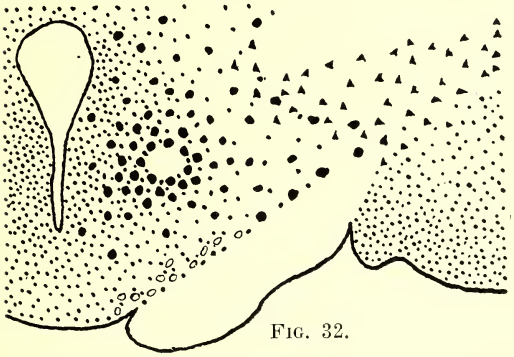


FIG. 32.

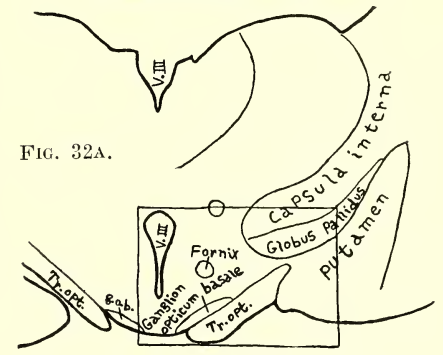


FIG. 32A.

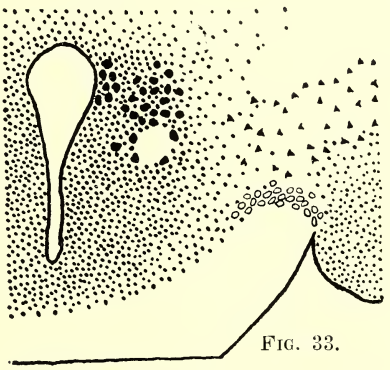


FIG. 33.

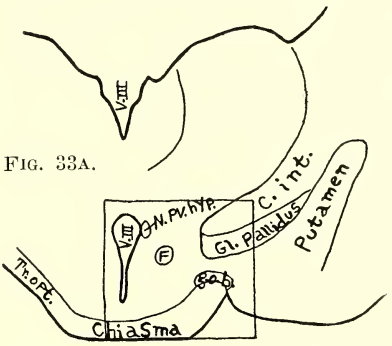


FIG. 33A.

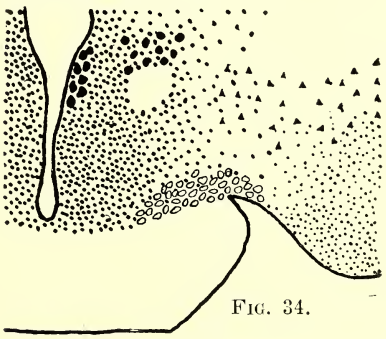


FIG. 34.

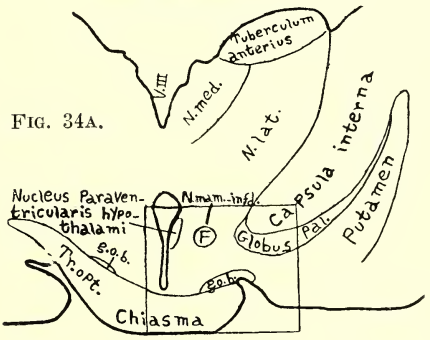


FIG. 34A.

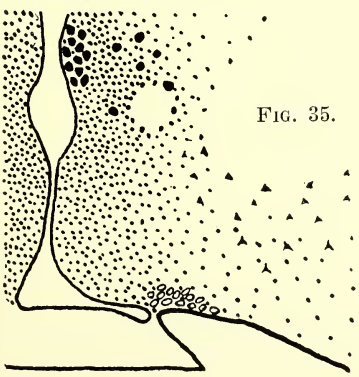


FIG. 35.

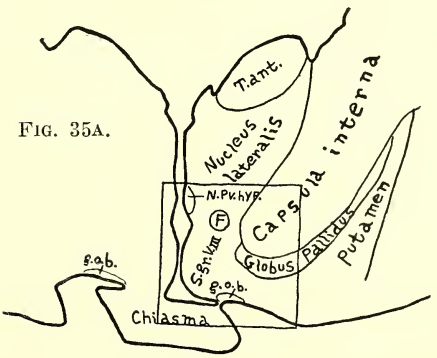


FIG. 35A.

PLATE X.

Homo. Series AC. Nuclei Tuberis Laterales.

Fig. 36 represents the actual appearance of a portion of the preparation from which Fig. 4 (Pl. I) was drawn. The preparation was projected at a magnification of 83½ diameters and every cell outlined in pencil. Then under the microscope each cell (as far as this was possible) was identified and reproduced in water color exactly as it appeared. This illustration is accordingly an accurate reproduction of the appearance of the preparation except that bloodvessels and neuroglia have been omitted.

Magnification (after ⅓ reduction) = 55⅔ diameters.

Comparing Fig. 36 with Figs. 4 and 4A it is evident that the region illustrated is the ventro-lateral portion of the tuber cinereum. At the right upper corner is seen a portion of the pes pedunculi, while at the left upper corner appears a portion of the fornix column.

The two groups of small pigmented cells are the nuclei tuberis laterales. Note that they are partly circumscribed by a zone containing few cells.

The large cells are those of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).

The small pale blue cells are those of the substantia grisea ventriculi tertii. Note transition types between these cells and the large cells of the nucleus tubero-mammillaris; this transition involves both the size of the cells and the intensity of the stain, so that some cells occur which could not be positively assigned to either of these two cell groups.

Compare the various cell groups of Fig. 36 with the corresponding cell types of Pl. XII, where the cells (man) are highly magnified.



PLATE XI.

HOMO. SERIES AC. GANGLION OPTICUM BASALE.

Fig. 37 shows the actual appearance of a portion of the basal optic ganglion in the preparation from which Fig. 9 (Plate III) was drawn. As in the case of Fig. 36 the preparation was projected (but at a magnification of 145 diameters instead of 83½) and every cell outlined in pencil. Then under the microscope every cell (except in rare instances where this was impossible) was identified and reproduced accurately in water color.

Magnification (after ⅓ reduction) = 96⅔ diameters.

Fig. 37 represents the whole breadth of the basal optic ganglion near its medial pole (Fig. 9, Pl. III), and shows the relation of this nucleus to the substantia grisea of the third ventricle. To the right is seen the ventrolateral surface of the brain (anterior perforated substance).

The large deeply staining cells are those of the basal optic ganglion. Note that it is sharply separated from the substantia grisea. The long coarse processes of the cells of the basal optic ganglion are here represented as blue, but in reality they are almost colorless; this figure, however, represents correctly the peculiar appearance of an intercellular feltwork, to which these processes give rise.

The small pale cells are those of the substantia grisea ventriculi tertii. Note the difference in appearance of the intercellular substance from that within the basal optic ganglion, due to the absence of coarse cell processes.

As in Fig. 36 bloodvessels and neuroglia have not been drawn.

See Pl. XII for the appearance of these two cell types (in man) under higher magnification.

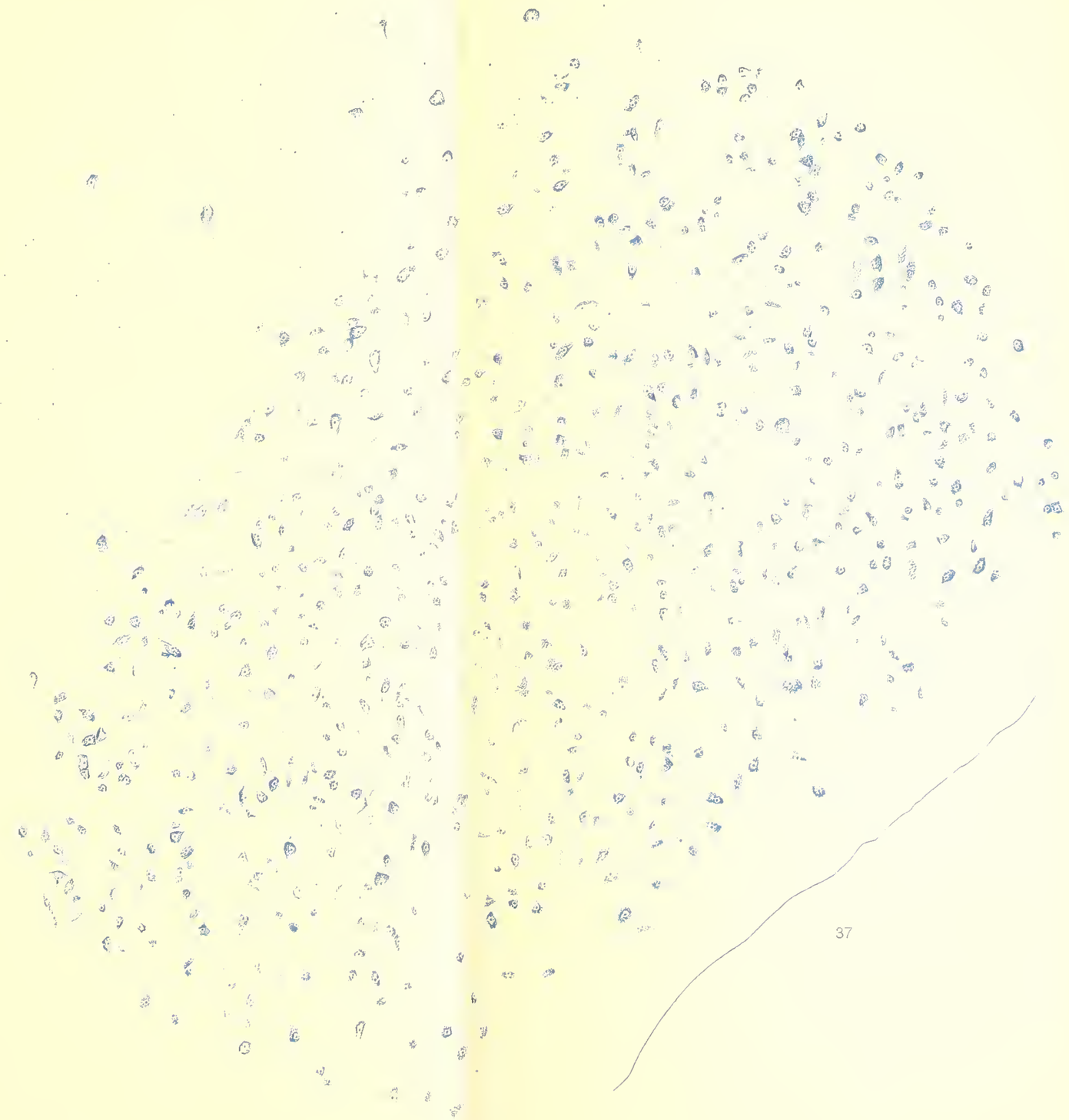
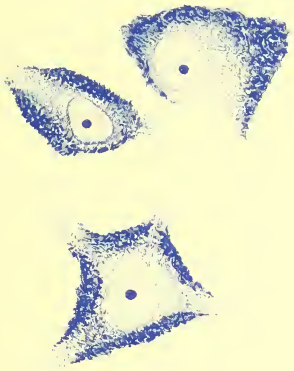


PLATE XII.

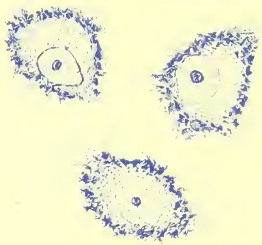
HOMO. MAGNIFICATION = 580 DIAMETERS.

38. Cells of the ganglion opticum basale.
39. Cells of the nuclei tuberis laterales.
40. Cells of the substantia grisea ventriculi tertii.
41. Cells of the nucleus tubero-mammillaris (formerly known as nucleus mammillo-infundibularis).
42. Cells of the nucleus ansae peduncularis (also known as ganglion basale of Kölliker).
43. Cells of the nucleus paraventricularis hypothalami.

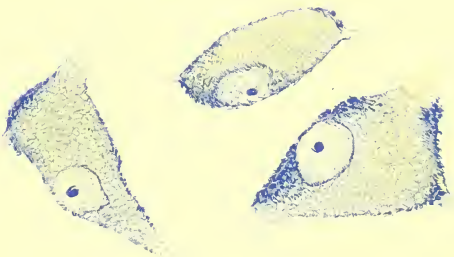
38



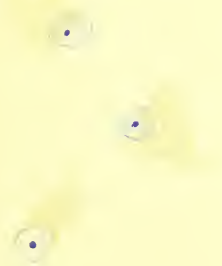
41



42



39



40



43

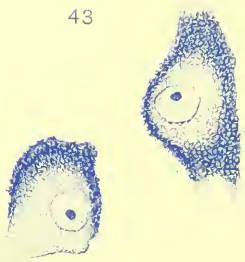
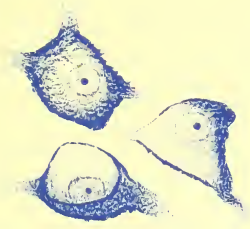


PLATE XIII.

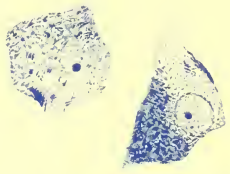
MACACUS RHESUS. MAGNIFICATION = 580 DIAMETERS.

44. Cells of the ganglion opticum basale.
45. Cells of the nuclei tuberis laterales.
46. Cells of the substantia grisea ventriculi tertii.
47. Cells of the nucleus tubero-mammillaris (formerly known as nucleus mammillo-infundibularis).
48. Cells of the nucleus ansae peduncularis (also known as the ganglion basale of Kölliker).
49. Cells of the nucleus paraventricularis hypothalami.

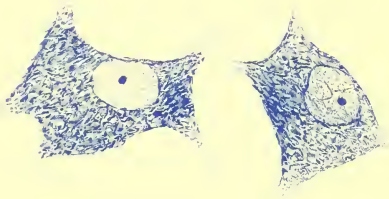
44



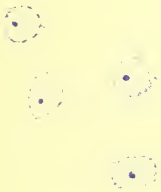
47



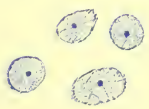
48



45



46



49

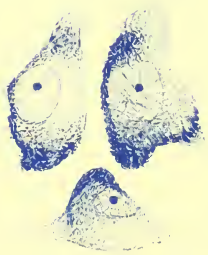
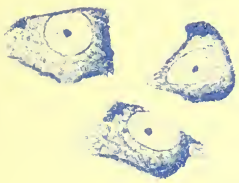


PLATE XIV.

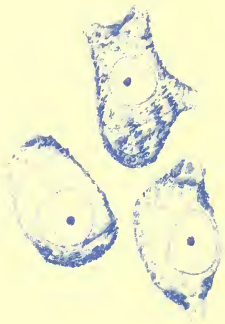
LEMUR RUFUS. MAGNIFICATION = 580 DIAMETERS.

50. Cells of the ganglion opticum basale.
51. Cells of the substantia grisea ventriculi tertii.
52. Cells of the nucleus tubero-mammillaris (formerly known as the nucleus mammillo-infundibularis).
53. Cells of the nucleus ansae peduncularis (also known as the ganglion basale of Kölliker).
54. Cells of the nucleus paraventricularis hypothalami.

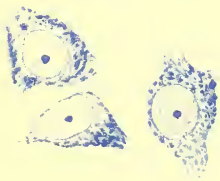
50



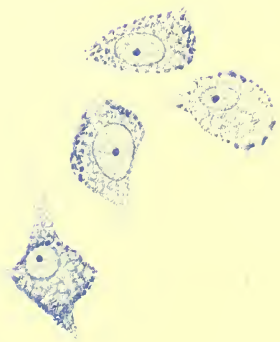
53



52



54



51

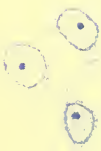


PLATE XV.

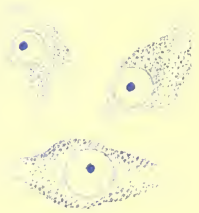
Cat. Magnification = 580 Diameters.

55. Cells of the ganglion opticum basale.
56. Cells of the substantia grisea ventriculi tertii.
57. Cells of the nucleus tubero-mammillaris (formerly known as the nucleus mammillo-infundibularis).
58. Cells of the nucleus paraventricularis hypothalami.

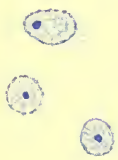
55



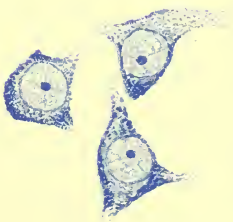
57



56



58



SEPARATE MONOGRAPHS REPRINTED FROM THE JOHNS HOPKINS HOSPITAL REPORTS.

Studies in Dermatology. By T. C. Gilchrist, M. D., and Emmet Rixford, M. D. 164 pages and 41 plates. Price, in paper, $3.00.

The Malarial Fevers of Baltimore. By W. S. Thayer, M. D., and J. Hewetson, M. D. And **A Study of some Fatal Cases of Malaria.** By Lewellys F. Barker, M. B. 280 pages. Price, in paper, $2.75.

The Pathology of Toxalbumin Intoxications. By Simon Flexner, M. D. 150 pages with 4 lithographs. Price, in paper, $2.00.

Studies in Typhoid Fever, I, II, III. By William Osler, M. D., and others. Extracted from Vols. IV, V and VIII of the Reports. 757 pages. Price, in cloth, $5.00.

Pneumothorax. A Historical, Clinical, and Experimental Study. By Charles P. Emerson, M. D. Price, in paper, $4.00.

NEW SERIES.

I. **Free Thrombi and Ball-Thrombi in the Heart.** By J. H. Hewitt, M. D. 82 pages and 20 illustrations. Price, in paper, $1.00.

II. **Benzol as a Leucotoxin.** By Laurence Selling, M. D. 60 pages and 3 plates, 1 in colors. Price, in paper, $1.00.

III. **Primary Carcinoma of the Liver.** By M. C. Winternitz, M. D. 42 pages. Price, in paper, 75 cents.

IV. **The Statistical Experience Data of The Johns Hopkins Hospital, Baltimore, Md., 1892-1911.** By Frederick L. Hoffman, LL. D., F. S. S. 161 pages. Price, in paper, $2.00.

V. **The Origin and Development of the Lymphatic System.** By Florence R. Sabin. 94 pages. Price, in paper, $2.00.

VI. **The Nuclei Tuberis Laterales and the So-called Ganglion Opticum Basale.** By Edward F. Malone. 70 pages and 15 plates. Price, in paper, $1.00.